DOES NOT CIRCULATE
UNIVERSITY OF MICHIGAN
JAN 24 1957
MEDICAL LIBRARY

The Journal of The SOUTH CAROLINA Medical Association

VOLUME LIII | JANUARY, 1957 | NUMBER 1

--- FEATURES ---

Fat, Blood, and Vascular Disease ..... Higginbotham and Williams

Potassium Metabolism in Surgery ..... L. B. Jenkins

Ammonium Toxicity ..... K. Roberts, et al

MEDICAL COLLEGE CLINICS

Vectocardiogram ..... J. A. Boone

Supine Hypotensive Syndrome ..... E. J. Dennis

SPECIAL ARTICLES

Cleft Palate Center — Tuberculosis in South Carolina

QUIETS AN AGITATED COUGH REFLEX

• SYRUP

DOLOPHINE HYDROCHLORIDE

(Methadone Hydrochloride, Lilly)

more effective in smaller doses than opium derivatives

Dosage: 1 teaspoonful; repeated only when necessary.

Palatable, cherry-flavored Syrup 'Dolophine Hydrochloride,' 10 mg. per 30 cc., is supplied in bottles of one pint and one gallon.

• Narcotic order required.

ELI LILLY AND COMPANY • INDIANAPOLIS 6, INDIANA, U.S.A.

Lilly
QUALITY / RESEARCH / INTEGRITY

YOUR PATIENT NEEDS AN ORGANOMERCURIAL

Practicing physicians know that many years of clinical and laboratory experience with any medication are the only real test of its efficacy and safety.

Among available, effective diuretics, the organomercurials have behind them over three decades of successful clinical use. Their clinical background and thousands of reports in the literature testify to the value of the organomercurial diuretics.

TABLET

NEOHYDRIN®

BRAND OF CHLORMERODRIN (10.3 MG. OF 3-CHLOROMERCURI-2-METHOXY-PROPYLUREA EQUIVALENT TO 10 MG. OF NON-IONIC MERCURY IN EACH TABLET)

a standard for initial control of severe failure

MERCUHYDRIN® SODIUM
BRAND OF MERALLURIDE INJECTION

LAKESIDE

02134

The Journal of The
SOUTH CAROLINA
Medical Association

JANUARY 1957 — VOL. LIII NO. 1

CONTENTS

EDITOR

JOSEPH I. WARING, M. D.
82 Rutledge Avenue
Charleston, S. C.

EDITORIAL BOARD

J. P. CAIN
J. D. GUESS
C. J. MILLING
H. R. PRATT-THOMAS
VINCE MOSELEY
BEN MILLER
W. H. PRIOLEAU
J. W. JERVEY
G. D. JOHNSON
R. M. POLLITZER
HUGH SMITH
WALTER MEAD

BUSINESS MANAGER

MRS. C. G. WATSON
105 W. Cheves Street
Florence, S. C.

SOUTH CAROLINA MEDICAL ASSOCIATION OFFICERS 1955-1956

WILLIAM H. PRIOLEAU, President
A. R. JOHNSTON, Vice President
D. L. SMITH, President-Elect
ROBERT WILSON, Secretary
HOWARD STOKES, Treasurer

COUNCILORS

BACHMAN SMITH, 1st District
A. F. BURNSIDE, 2nd District
H. B. MORGAN, 3rd District
C. N. WYATT, 4th District
R. L. CRAWFORD, 5th District
J. P. CAIN, 6th District
A. C. BOZARD, 7th District
J. H. GRESSETTE, 8th District
J. M. FLEMMING, 9th District

DELEGATES TO THE AMERICAN MEDICAL ASSOCIATION

Delegates
WILLIAM WESTON, JR.
GEORGE DEAN JOHNSON
Alternates
ROBERT WILSON
C. N. WYATT

EXECUTIVE SECRETARY

MR. M. L. MEADORS
120 W. Cheves Street
Florence, S. C.

THE JOURNAL OF THE SOUTH CAROLINA MEDICAL ASSOCIATION—Published monthly by The South Carolina Medical Association, 105 West Cheves Street, Florence, South Carolina. Subscription Price: $3.00 a Year. Entered as second-class matter February 9, 1916, at the post office at Greenville, South Carolina, under Act of March 3, 1879. Accepted for mailing at special rate of postage provided for in Sec. 1103 Act of October 3, 1917, authorized Aug. 2, 1918.

ORIGINAL ARTICLES

Intravascular Agglutination of The Blood Following Fat Ingestion—*A. Curtis Higginbotham, Ph. D. and Arthur V. Williams, M. D.* ... 1

Surgical Interest In Fluids and Electrolytes—*Louie B. Jenkins, M. D.* ... 10

Ammonium Toxicity—*Kathleen E. Roberts, Parker Vanamee, John Jacquez, Walter Lawrence, Jr., and J. William Poppell* ... 16

MEDICAL COLLEGE CLINICS

Electrocardiogram of The Month—The Vectorcardiogram—*John A. Boone, M. D.* ... 22

Supine Hypotensive Syndrome—A Case Report—*Edward J. Dennis, M. D.* ... 23

SPECIAL ARTICLES

The Cleft Lip and Cleft Palate Center, Medical College of South Carolina—*Robert F. Hagerty, M. D.* ... 32

Tuberculosis in South Carolina Today—*Frank L. Geiger, M. D.* ... 33

EDITORIALS

Old Age, A Service Connected Disability ... 26

Once More The Polio Vaccine ... 26

Community And Other Fund Campaigns ... 26

Foundation For Eye Care ... 27

AMA Studies Uniform Chemical Labeling Law ... 27

Your Journal ... 28

FEATURES

President's Page ... 25

Blue Cross—Blue Shield ... 29

South Carolina Chapter American Academy of General Practice ... 30

News ... 34

Announcements ... 36

Deaths ... 36

Book Reviews ... 36

Contributions of Original Articles

Length of Article—Ordinarily articles should not exceed 3,000 words (approximately 3 printed pages). Under exceptional circumstances only will articles of over 4,000 words be published.

Manuscripts—Manuscripts should be typewritten, double spaced, and the original and a carbon copy submitted.

Illustrations—Ordinarily publication of 2 or 3 illustrations accompanying an article will be paid for by THE JOURNAL. Any number beyond this should be paid for by the author.

References—Should conform to the following order: name of author, title of article, name of periodical, with volume, page, month, day of the month if weekly, and year—e. g.: Lee, G. S.: The heart rhythm following therapy with digitalis, Arch. Int. Med., 44:554, Dec. 1942. They should be listed in alphabetical order and numbered in sequence.

Reprints—Reprints will be made for the author at established standard rates.

Erythromycin in Treating Pneumonia

A 27-year-old man, a chronic alcoholic, was admitted with a history of an alcoholic spree followed by a cough, greenish sputum and chills and fever.

Physical examination showed a temperature of 104 F. and indicated pneumonia in the right lower lobe. This was confirmed by X-ray. The sputum revealed gram-positive diplococci and blood culture subsequently grew Type VII pneumococci.

The patient was treated with erythromycin, 300 mg. every six hours per os. His temperature dropped to normal by 48 hours and X-ray of the chest revealed considerable clearing by the fourth hospital day. After 10 days hospitalization, the patient was fit for discharge.[1]

First Antibiotics Symposium, we reported the successful treatment with hromycin of *H. influenzae* pneumonia and bacteremia. A second patient with *H. influenzae* pneumonia and bacteremia had a clinical course almost identical to the one previously reported, with cure obtained by treatment with 500 mg. of erythromycin per os every four hours for 14 days.

Of these 132 patients with bacterial pneumonia, 127 (96%) had a good clinical result. One patient with lobar pneumonia had a good initial
delayed resolution

The Journal
of the
South Carolina Medical Association

VOLUME LIII January, 1957 NUMBER 1

INTRAVASCULAR AGGLUTINATION OF THE BLOOD FOLLOWING FAT INGESTION

A POSSIBLE FACTOR IN THE PRODUCTION OF ANGINA PECTORIS AND CORONARY THROMBOSES, AND IN THE PATHOGENESIS OF ATHEROSCLEROSIS

A. CURTIS HIGGINBOTHAM, Ph. D. AND ARTHUR V. WILLIAMS, M. D.
Charleston, South Carolina

INTRODUCTION

Many clinical, pathological and experimental studies implicate the lipids (fat and fat-like substances), especially cholesterol, in the etiology of atherosclerosis.[1-7] The observation that mortality from heart disease in some populations decreases when the fat content of the diet is reduced, and then immediately returns to former levels when it is restored, suggests that the fat has an immediate effect on coronary disease.[6,7] Supporting evidence for this view comes from studies showing an increase in the frequency of anginal attacks and coronary thromboses in groups of coronary patients on high fat diets and a decrease in those on low fat diets,[8,9] and of the induction of angina pectoris by the ingestion of fatty test meals.[10]

We have observed changes in the blood and blood vessels of the bulbar conjunctiva following ingestion of fat-enriched meals which we believe to be part of the mechanisms involved in the production of the syndromes of coronary disease, and in the progression of atherosclerosis.

The mechanisms whereby fatty diets or single fat meals produce these immediate effects on the blood and blood vessels, and the relationships of these changes to angina pectoris and coronary thrombosis, have not been completely described. How these blood-vascular alterations may contribute to the pathogenesis of atherosclerosis is as yet an unanswered question.

This paper has two purposes. The first is to describe experiments and observations recording certain microscopically visible changes occurring in the blood and small blood vessels of some people following the ingestion of a fat-enriched meal.* The second is to use these observations, and those reported by other investigators, as a basis for considering intravascular agglutination of the blood** and postprandial lipemia as factors in the production of angina pectoris and coronary thrombosis, and in the pathogenesis of atherosclerosis.

From the Departments of Anatomy and Medicine, Medical College of South Carolina.

This work was aided by Navy Grant Nonr-434(01), USPHS Grant H-1020(C3), and The John A. Hartford Foundation, Inc.

*Only the most obvious vessel pathology (e.g. sacculations) were recorded in this study. For precise descriptions of the responses of small blood vessels to increasing degrees of injury, see Clark, E. R. and Clark, E. L.: Changes in the blood vascular endothelium in the living animal. Am. J. Anat., *57*: 385, 1935; and Brooks, F. H.; Dragstedt, L., Warner, L., and Knisely, M. H.: Sludged blood following severe thermal burns. Arch. Surg., *61*: 387, 1950.

**"Intravascular agglutination of the blood" as used in this paper is intended to mean the same as the term "sludged blood" introduced by Knisely to designate the sticking together of the formed elements of the blood to form a suspension which is more difficult to pump through the small blood vessels than normal unagglutinated blood.

For an introductory bibliography concerning the concepts of healthy normal blood, of sludged blood, and of some effects of sludged blood on the bodies of animals and men, see An Annotated Bibliography on Sludged Blood by Melvin H. Knisely, Postgraduate Medicine, *10*: 15-93, 1951.

METHODS

Two groups of patients were studied. The first included those suffering from angina pectoris, and the second having a variety of either cardiovascular or metabolic diseases or both. Ten apparently healthy male medical students constituted a third group.

Microscopic studies of the blood and blood vessels were carried out on the bulbar conjunctiva, following a period of fasting (usually over night), and following a high fat meal, during the postprandial absorptive period at the time of expected peak lipemia.[10,11] Each individual thus served as his own control, since we were interested primarily in changes which had occurred following the test meals.

The observations were made using a modification of the method of Knisely, Bloch, Eliot, and Warner[12] which permits observations of (a) a sample of the circulating arterial blood arriving in the vascular bed of the bulbar conjunctiva; (b) visible changes, if any, in the blood as it passes through the bed; and (c) some of the responses and structural features of the blood vessels.

Two modifications of the eye method were used. A 40-watt zircon arc lamp (manufactured by Fish-Schurman Corporation, New Rochelle, New York) was used to illuminate the bulbar conjunctiva obliquely (Fig. 1). On some occasions, the light falling on the bulbar conjunctiva was polarized. A light polarizing filter, either Polaroid or a Nicol prism, was fastened on the front of the zircon arc lamp in the beam of light passing from the lamp to the conjunctiva. The use of polarized light permitted clear, direct observations of the blood in subsurface vessels.

A Leitz biobjective stereobinocular microscope was used with magnifications of 50X to 150X.

RESULTS

The results are presented in three parts. The first contains the case history, experimental procedure, and detailed observations of one patient in the first group studied. This is followed by a chart recording in abbreviated form the results of similar studies of the ten patients in this group. The second is a general discussion of the blood vascular changes following fat ingestion observed in patients hospitalized with a variety of cardiovascular and metabolic diseases. The third describes the effects of a single high fat meal noted in apparently normal, healthy medical students.

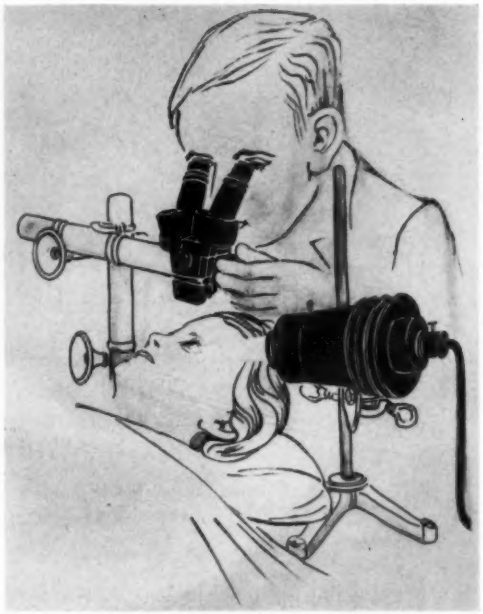


Figure 1.—Drawing illustrating method of observing a patient's bulbar conjunctiva. Patient is in a supine position. A bright beam of light from a laterally-placed lamp is focused on the bulbar conjunctiva. Low power (2X) objectives and 12.5X oculars are portrayed here. Higher powered objectives (up to 12X), giving magnification up to 150 diameters, can be used.

Case History: Patient No. 1, a 44-year old white male welder, was first seen in January, 1953, his chief complaint being "a heart murmur". Past history was non-contributory.

Positive physical findings were limited to the heart. Sinus rhythm was present at a rate of 72. There was a Grade II blowing systolic aortic murmur, and a Grade I-II blowing systolic mitral murmur. His electrocardiogram was within normal limits. Cardiac fluoroscopy showed minimal left ventricular hypertrophy. The clinical impression at that time was rheumatic heart disease with aortic stenosis and mitral insufficiency, functional classification I.

The patient remained asymptomatic until November, 1955, when he was next seen because of the sudden onset of substernal pain, radiating to both shoulders, and persisting for

approximately one hour. His physical findings were unchanged, but the electrocardiogram showed sharp inversion of the left precordial T waves, and the T waves in standard leads 1, 2, and AVL, indicative of myocardial ischemia. Cardiac fluoroscopy again revealed minimal left ventricular enlargement.

The patient was hospitalized, and put on a low fat diet and Dicumarol (Bishydroxycumarin). Substernal pain, radiating to both shoulders, continued during the first few days of his hospitalization. Two weeks after admission, and following an over night fast, study of the blood and blood vessels in the bulbar conjunctiva revealed a very mild degree (1+)* of intravascular agglutination. The masses of agglutinated cells were very small, each consisting of a few cells, and just barely visible in the venules at a magnification of 50X. No plugging of vessels was observed.

He then ate a breakfast of eggs, ham, buttered toast, and coffee with cream, containing an estimated total of 160 grams of fat.

Microscopic study was resumed six hours after the ingestion of this high-fat breakfast. There was an easily noticeable increase in the degree of agglutination of his erythrocytes (from 1+ to 3+). The red cell masses in the venules were considerably larger than those present in the morning before he had eaten breakfast. The masses were larger in diameter and easily seen at magnification of 50X. Many of them were several times as long as the diameters of the vessels in which they were located. Several terminal arterioles were intermittently plugged by visible masses. There was complete, "transient stasis" in many of the capillaries and small cross-connecting venules. By this we mean that vessels contained soft masses of agglutinated cells which stood perfectly still from 5 to 20 seconds or longer. Upon entering the venules, these masses sometimes would combine to form larger masses. All the visible moving blood was passing along much more slowly than before the ingestion of the high-fat meal.

*The photographs of the bulbar conjunctivae in Figure 3 illustrate some of the characteristics of the various degrees (1+, 2+, etc.) of intravascular agglutination. For further details see footnote for Table I.

About three hours following this period of observation, the patient again complained of substernal pain of the anginal type, radiating to his left shoulder. An electrocardiogram made at this time showed inversion of the T waves in the left precordial leads (Fig. 2A). The patient's pain was present intermittently during that afternoon and early evening, but disappeared during the night. An electrocardiogram made the next morning showed upright T waves in the left precordial leads (Fig. 2B).

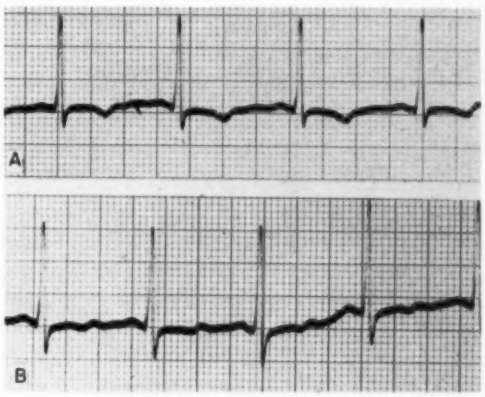


Figure 2.—Lead V5 of an ECG made on patient No. 1. a. During the anginal pain which followed the fat-loaded breakfast and the increased intravascular agglutination of the blood. Note the inverted T waves. b. Following the high fat breakfast, after the anginal pain had subsided. The T waves are now upright.

The patient was placed on a low fat diet, and has returned to work as a welder. He had no further symptoms since his discharge from the hospital in October, 1955, until January, 1956, when he again began having anginal attacks.

The results of study of the ten patients in this group are recorded in Table I. Patient 1 is included in the chart to show how the findings are recorded. Instead of fatty foods, some patients drank "milk shakes" (1 pint of homogenized milk with 3 scoops of vanilla ice cream) enriched with Ediol,* a cocoanut oil liquid fat preparation containing 50 grams of fat per 100 cc. In all patients except 7 and 9, there was a microscopically detectable increase

*Prepared by the Schenley Laboratories, Inc.

in the degree of agglutination of the circulating blood following the ingestion of a single fatty meal. The agglutinated masses were easily seen at 50X. In addition to Patient 1, Patients 3 and 8 developed severely agglutinated blood in parts of their bulbar conjunctiva

Table I. Summary of changes following fat ingestion observed in the blood and blood vessels of patients suffering from angina.

Patient No.	Sex and Age	Diagnosis	Blood pressure	Relevant Symptomatology	Most severe degree of IV Agg. seen before fat*	Kind of fat fed	Most severe degree of IV Agg. after fat	Angina after fat
1.	m/44	Recent infarc.	130/85	Angina (see case history)	1+	Fatty breakfast	3+	Yes
2.	m/40	Coronary atherosc. Peptic ulcer	140/90	Angina of effort	1+	Ediol	2+	No
3.	f/44	Coronary atherosc.	140/80	Angina of effort	1+	Ediol	3+	Yes
4.	m/59	Coronary atherosc. Old infarc. Diabetes mellitus	160/90	0	2+	Ediol	3+	No
5.	m/52	Coronary atherosc.	145/85	Angina of effort	1+	Fatty breakfast	2+	No
6.	m/45	Post-infarc.	130/80	0	2+	Fatty breakfast & Ediol	3+	No
7.	m/44	Coronary atherosc. Post-infarc.	140/90	Angina of effort	1+	Fatty breakfast & Ediol	1+	No
8.	m/54	Recent infarc.	120/70	0	1+	Ediol	3+	Yes
9.	m/74	Coronary atherosc.	110/70	Mild angina of effort	2+	Ediol and cream	2+	No
10.	m/67	Coronary atherosc.	150/65	Mild angina of effort	1+	Pint of whipping cream	2+	No

*IV Aggl. denotes intravascular agglutination of the blood. The most severe degree observed in any area of the bulbar conjunctival vascular bed is the one recorded.

The degrees of intravascular agglutination of the blood are indicated as 1+, 2+, 3+, and 4+. The most severe vessel injury generally was associated with the most severely agglutinated blood. The distinguishing criteria for each degree of agglutination as viewed at a magnification of 50X are as follows:

1+ Mildly agglutinated blood. Masses small, barely visible in some venules. Venular flow tending to be non-laminar. Capillary flow continuous.

2+ Moderately agglutinated blood. Masses larger and visible in all venules. Occasional pliable, elongated masses pass through some capillaries. Transient plugging of terminal arterioles. Venular masses tend to combine to form larger masses, especially in the relatively short vessels connecting two venules. Occasional fusiform sacculation of venular walls. Flow through venules slower than that of unagglutinated blood.

3+ Moderately severe agglutinated blood. Masses of various sizes in all venules. Largest ones in venules through which flow is slow or temporarily halted. The length of some of the largest masses may be several times the diameter of the venule in which they are located. Slow passage of pliable elongated masses through most patent capillaries at irregular intervals. Some occasional brief plugging of arterioles. Fusiform sacculation of venules common. Occasional conspicuous lateral sacculations of venules. "Temporary stasis" common in venules of some areas. Flow decidedly slower through areas with most severe agglutination.

4+ Severely agglutinated blood. Many venules containing large, slow-moving masses. Some venules impacted with stationary masses, or masses which occasionally move. Virtually no laminar flow in venules. Brief plugging of arterioles common, some appearing "permanently" plugged. "Stranded" masses in many capillaries. Flow through entire vascular bed very slow.

and later experienced anginal pain. These two patients also had "transient" stasis in many of the capillaries and venules. Temporary plugging of the small vessels occurred quite often during the observational period. No patient in this group developed anginal pain without previously having intravascular agglutination of the blood, reduced blood flow, and plugging of some of the conjunctival vessels.

Because of the increase in agglutination of the blood, altered blood flow and increased vessel damage observed in the majority of these patients following fat ingestion, we wanted to determine if these changes occurred in other patients tested in a similar manner. Accordingly, patients with a variety of cardiovascular and metabolic diseases (regardless of history of coronary disease) were studied in the Vascular Clinic of Roper Hospital and the Medical College Teaching Hospital. In many of these patients, the initial degree of agglutination was so severe and the blood flow and vessel structure so abnormal that we did not detect additional changes after fat ingestion by our method. This was true especially of patients known to have deranged lipid metabolism (Fig. 3C). In others, the ingestion of fatty test meals brought about changes similar to those observed in the first group studied. (See Fig. 3B for an example of a sacculated venule.)

We also wanted to know if these changes occurred in healthy people after fat ingestion. Each of a group of 10 apparently healthy male freshman medical students were studied after an over night fast, and again during the period of expected peak of dietary lipemia following the drinking of a fat-enriched (Ediol) milk shake (Table II).

No changes in the degree of agglutination and flow of the blood, and vessel pathology were observed in three of the 10 students. Two of the three had agglutinated blood, slow nonlaminar blood flow in some venules and a few venular sacculations. Failure to detect changes also occurred with some of the patients.

Changes were observed in the other seven students. The degree of agglutination of the blood increased noticeably in six, but increase in the pathologic appearance of the vessel was seen in only three. One had increase in vessel pathology but no noticeable increase in agglutination.

Table II. Summary of effects of fat ingestion on the blood and blood vessels in the bulbar conjunctiva of medical students.

Student No.	Sex and Age	Most severe degree of IV Agg. seen before fat*	Most severe degree of IV Agg. after fat
1	m/21	2+	2+
2	m/22	2+	3+
3	m/30	3+	3+
4	m/22	1+	2+
5	m/23	1+	1+
6	m/22	3+	3+
7	m/22	2+	3+
8	m/22	1+	2+
9	m/22	0	1+
10	m/25	2+	3+

*See footnote for Table I.

DISCUSSION

Dietary fat seems to be an important etiological factor in the production of angina in patients with severe coronary atherosclerosis. Fat ingestion in most of those we studied was followed by a detectable increase in the agglutination of the blood and reduced blood flow. Angina occurred in three. Dietary fat also appears to be an important factor in the progression of atherosclerosis since the reduced blood flow probably plays an important role in "setting the stage" for embolization and rupture of capillaries in atherosclerotic plaques. The resulting hemorrhages have been thought to cause coronary insufficiency by enlargement of the plaques in some cases, and coronary thrombosis in others.[13-15]

Ingestion of a fat-enriched meal produces lipemia in both animals[16] and man.[10,11] The degree of the lipemia is difficult to predict because it varies considerably with the amount of fat ingested, the age of the individual, the state of health, and many other factors.

Intravascular agglutination of the blood cells occurs in hamsters and man following the ingestion of considerable quantities of fat.[16,17] In hamsters the degree of the agglutination is proportional to the degree of the lipemia. (The degree of lipemia was not determined in the people we studied.)

In addition to its increased agglutination

and altered chemical composition, lipemic blood differs in some other respects from non-lipemic blood. Swank[18] reported an increase in the viscosity of the blood of hamsters following the ingestion of fatty test meals. Fullerton, Davie, and Anastasopoulos[19] found that lipemic blood has a shorter clotting time. It has a decreased sedimentation rate.[20]

Our observations of altered blood rheology and pathogenic changes in blood vessels associated with agglutinated blood agree with those of Knisely et al.[21-23] Not all of the changes were observed in the same patient, nor were they present in the same degree in every patient. The changes were not uniform in all parts of the bulbar conjunctival vascular bed. For example the blood in the venules draining the capillaries of one area could be severely agglutinated and flowing very slowly while those in other areas contained less severely agglutinated and faster flowing blood. The differences between patients may be due in part to the different chemical composition of the plasma, the degree of agglutination of the blood being delivered to the bulbar conjunctiva, and the condition and degree of response of the small vessels.

The arterial blood delivered into the vascu-

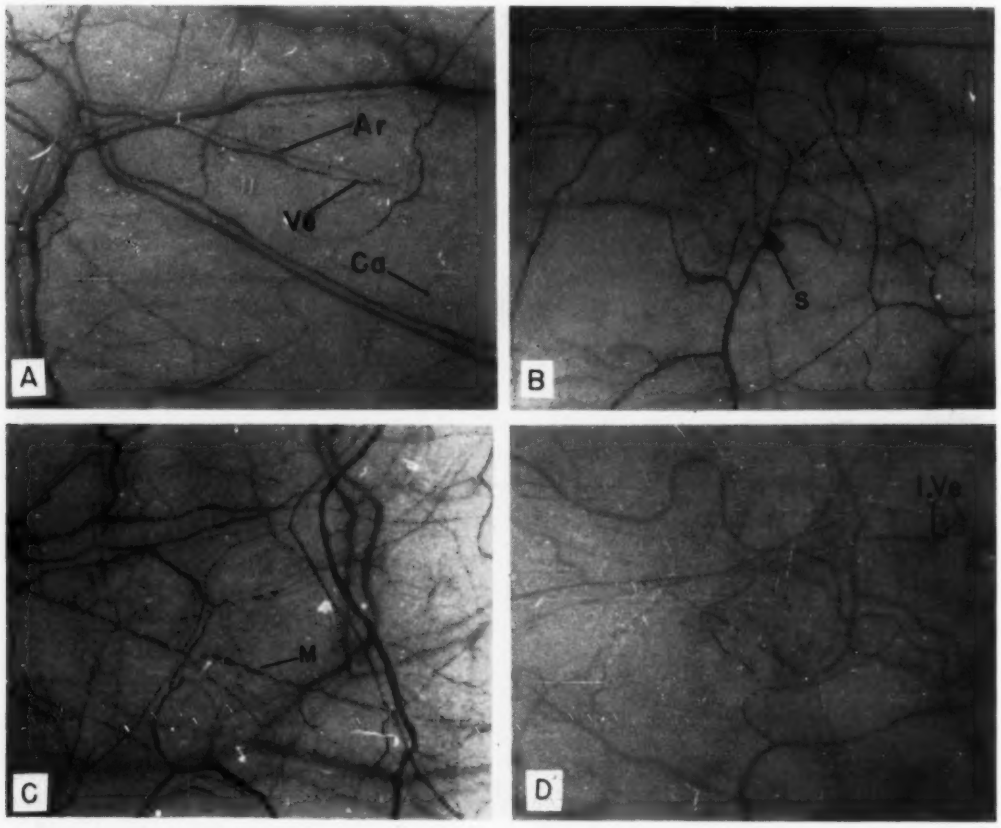


Figure 3.—Photographs of the bulbar conjunctival vessels illustrating various degrees of agglutinated blood and some vessel change. See footnote to Table I for further details.
a. Mildly (1+) agglutinated blood and no visible vessel pathology. Ar = arteriole. Ve = venule. Ca = capillary.
b. Moderately (2+) agglutinated blood. Note large lateral venular sacculation (S).
c. Moderately severe (3+) agglutinated blood. Note large masses of agglutinated blood cells (M) in a venule.
d. Severely (4+) agglutinated blood. Note vessel (I.Ve.) impacted with large masses of agglutinated cells.

lar bed of the bulbar conjunctiva has been considered a valid sample of the arterial blood distributed peripherally by the aorta.[12,24,25] This may not always be true for people who have ulcerated atherosclerotic plaques in some arteries and not in others. The properties of the blood may be modified as it passes over such lesions.[13,26] Knisely et al[27] saw blood agglutinate as it flowed through slightly traumatized vessels. Blood entering the vascular bed of the myocardium from atherosclerotic coronary arteries, therefore, may be agglutinated to a greater degree, or have more tendency to agglutinate, than that being delivered to the bulbar conjunctiva.

The flow characteristics of agglutinated blood *in vitro* and *in vivo* are not the same as those of unagglutinated blood,[22,28,29] As the agglutinated blood flows through long tapering cone-like arteries, its linear velocity decreases, in part because of the irregular tumbling, shearing, and deformation of the agglutinated masses as they pass into and tend to plug vessels with progressively decreasing diameters. The increased resistance to flow of lipemic blood[18] may be due in part to numerous chylomicrons as well as to agglutinated masses of blood cells. Irregularities in the lumens of the arteries, such as sacculations and partial occlusions, by increasing turbulence, should accentuate the deceleration of the blood flow. As a consequence, the effective blood pressure in the terminal arterioles should be reduced, some small vessels become plugged (transiently at least), and the total blood flow through the capillaries should be decreased.

The exchange rates of metabolites between the blood and adjacent tissues are reduced by decreasing the volumetric rate of blood flow through the capillary.[30-35] Because of the decreased rate of blood flow through the myocardial vascular bed with subsequent reduced metabolic exchange rates, agglutinated blood associated with postprandial lipemia may be a direct-acting contributory factor in producing myocardial ischemia and angina in patients with an already severely restricted coronary blood flow.

In our series of patients, and in those reported by Kuo and Joyner,[10] the onset of angina pectoris occurred three to five hours or more following the ingestion of a fatty meal. The close correspondence of the onset of anginal attacks to the peak or expected peak of the postprandial lipemia suggests that the lipemia, or something associated with it, is involved.

Agglutinated blood may flow so slowly through capillaries and venules that the endothelium of these vessels becomes hypofunctional and damaged. The longer the duration of reduced flow, the greater will be the derangement of function and resulting damage. Landis[36] and Maurer[37] found that reducing the supply of oxygen to capillaries caused them to leak excessive amounts of plasma proteins. O'Neill[38] demonstrated that the venous endothelium of a large vein could be severely damaged by occluding the venous vasa vasorum. Severe sclerosis with lipid deposition is known to follow various types of injury to artery walls (e.g., syphilitic aortitis, arterial cauterization, and ischemia produced by macromolecular substances), especially in conjunction with cholesterol feeding.[39] Knisely et al,[12] and Bloch[25,26] have described minute sacculations of vessel walls associated with agglutinated blood and reduced blood flow.

Paterson[13-15] studied the incidence of intramural hemorrhage in relation both to the progression of atherosclerosis and to coronary thrombosis. He described evidence purporting to show high frequency of minute hemorrhages of relatively long standing in certain plagues in addition to the more recent ones in other plaques. He expressed the opinion that rupture of the poorly supported, thin-walled capillaries (described by Wartman[26]) in the atherosclerotic plaques was an important contributory factor in enlargement of the plaques, and in coronary thrombosis. Should sacculations, like those which we have seen in the vascular bed of the bulbar conjunctiva (Fig. 3B), also form in the abnormal capillaries or venules of coronary atherosclerotic plaques, their rupture could produce intramural hemorrhages which could contribute to enlargement of the plaques, and lead to occlusion of the affected artery. Should the hemorrhaged blood

gain entrance into the lumens of coronary arteries, it could produce coronary thrombosis.[13,27]

SUMMARY AND CONCLUSIONS

Intravascular agglutination of the blood, reduced blood flow, and changes in vessel walls frequently follow fat ingestion by man. Nine of ten patients whose case histories indicated severe coronary atherosclerosis, when given a fat test meal, developed these blood-vascular changes, at a time corresponding to the peak of the expected postprandial lipemia. Anginal pain occurred in some instances.

Similar vascular changes occurred in other patients with a variety of cardiovascular and metabolic diseases following the ingestion of a fat test meal. In some, particularly those with metabolic diseases the initial intravascular agglutination and vessel pathology were so severe that no additional change was detectable by our methods. In a few who had only a mild initial agglutination and minimal or no vessel pathology, there was no detectable change.

Increase in intravascular agglutination, reduced blood flow, and alterations in the walls of small blood vessels were observed following a single fat-enriched meal in most of the healthy medical students similarly tested. The changes, however, were not as great as in the patients tested.

These changes in the blood-vascular system, which follow the ingestion of fat and are associated with the postprandial lipemia, very probably are important contributory factors in the production of some cases of angina pectoris, and in the pathogenesis of atherosclerosis, especially in people who regularly eat a diet high in fat.

The authors wish to thank the following members of the staffs of the Medical College of South Carolina, and Roper Hospital, for their generous assistance: Dr. Melvin H. Knisely, Professor and Chairman of the Department of Anatomy; Dr. J. Manly Stallworth, Assistant Professor of Surgery and Director of the Vascular Clinic; Dr. Edwin Boyle, Jr., Instructor in Medicine and Established Investigator of the American Heart Association; and Miss Ann B. Boone, R. N., of the Vascular Clinic.

REFERENCES

1. Hirsch, E. F., and Weinhouse, S.: The role of the lipids in atherosclerosis. Physiol. Rev., *23*:3, 1943.
2. Katz, L. N., and Stamler, J.: Experimental Atherosclerosis. Springfield, Ill., Charles C. Thomas. 1953.
3. Keys, A.: Human atherosclerosis and the diet. Circulation, *5*:115, 1952.
4. Moreton, J. R.: Chylomicronemia, fat tolerance and atherosclerosis. J. Lab. & Clin. Med., 35:373, 1950
5. Leary, T.: Crystalline ester cholesterol and atherosclerosis. Arch. Path., *47*:1, 1949.
6. Malmros, H.: The relation of nutrition to health—a statistical study of the effect of war-time on arteriosclerosis, cardiosclerosis, tuberculosis, and diabetes. Acta. Med. Scandinav., (*Suppl. 246*): 137, 1950.
7. Dedichen, J.; Strom, A., Jelsten-Jensen, R., and Closs, K.: Incidence of atherosclerotic disease during war years. Trans. Fifth Conf. on Factors Regulating Blood Pressure. New York, Josiah Macy, Jr. Foundation, p. 117, 1951.
8. Plotz, M.: Possible hazards of high fat diets in coronary disease. J.A.M.A., *139*:623, 1949.
9. Morrison, L. M.: A nutritional program for prolongation of life in coronary atherosclerosis. J.A.M.A., *159*:1425, 1955.
10. Kuo, P. T., and Joyner, C. R.: Angina pectoris induced by fat ingestion in patients with coronary artery disease. J.A.M.A., *158*:1008, 1955.
11. Becker, G. H.; Meyer, J., and Necheles, H.: Fat absorption and atherosclerosis. Science, *110*:529, 1949.
12. Knisely, M. H.; Bloch, E. H., Eliot, T. S., and Warner, L.: Blood: Circulating; Method and Apparatus In: Glasser, O.: (ed.) Medical Physics, Volume II. Chicago, Year Book Publishers, Inc., 1950.
13. Paterson, J. C.: Capillary rupture with intimal hemorrhage as a causative factor in coronary thrombosis. Arch. Path., 25:474, 1938.
14. Paterson, J. C.: Factors in the production of coronary artery disease. Circulation, *6*:732, 1952.
15. Paterson, J. C.: The reaction of the arterial wall to intramural hemorrhage. In: Symposium of Atherosclerosis, Publication 338 of National Academy of Sciences, National Research Council, 65-71, 1955.
16. Cullen, C. F., and Swank, R. L.: Intravascular aggregation and adhesiveness of the blood elements associated with alimentary lipemia and injections of large molecular substances. Circulation *9*:335, 1954.
17. Higginbotham, A. C.; Williams, A. V., and Knisely, M. H.: Some acute effects of dietary fat on intravascular agglutination in cardiac patients. Abstract. Anat. Rec., *121*:310, 1955.
18. Swank, R. L.: Effect of high fat feedings on viscosity of the blood. Science, *120*:427, 1954.
19. Fullerton, H. W.; Davie, W. J. A., and Anastasopoulos, G.: Relationship of alimentary lipaemia to blood coagulability. Brit. M. J., 2:250, 1953.
20. Swank, R. L.: Changes in blood produced by a fat meal and by intravenous heparin. Am. J. Physiol., *164*:798, 1951.
21. Knisely, M. H.; Stratman-Thomas, W. K., Eliot, T. S., and Bloch, E. H.: Knowlesi malaria in monkeys. I. Microscopic pathological circulatory physiology of rhesus monkeys during acute knowlesi malaria. J. Nat'l. Malaria Soc., *4*:285, 1945.

22. Jeffords, J. V., and Knisely, M. H.: Concerning the geometric shapes of arteries and arterioles. A contribution to the biophysics of health, disease, and death. Angiology, 7:105, 1956.
23. Saunders, E. A., and Knisely, M. H.: Living mesenteric terminal arterioles before and immediately after embolization. Measurement and comparison of internal diameters; a contribution to the biophysics of disease. Arch. Path., 58:309, 1954.
24. Bloch, E. H.: The bulbar conjunctiva of man as a site for the microscopic study of the circulation. First Conference on Microcirculatory Physiology and Pathology. Anat. Rec., *120*:349, 1954.
25. Bloch, E. H.: Microscopic observations of the circulating blood in the bulbar conjunctiva in man in health and disease. Ergebnisse d. Anatomie u. Entwicklungsgeschichte, *35*:1, 1956.
26. Wartman, W. B.: Vascularization and haemorrhage in the arterial wall. Studies in Pathology, presented to Peter MacCallum. Melbourne, University Press, 1950.
27. Knisely, M. H.; Eliot, T. S., and Bloch, E. H.: Sludged blood in traumatic shock. I. Microscopic observations of the precipitation and agglutination of blood flowing through vessels in crushed tissues. Arch. Surg., *51*:220, 1945.
28. Madow, B., and Bloch, E. H.: The effect of erythrocyte aggregation on the rheology of the blood. Angiology, 7:1, 1956.
29. Knisely, M. H.: Some factors in the rheology of unagglutinated and sludged blood in living blood vessels. Anat. Rec., *124*:320, 1956 (Abstract).
30. Bloch, I.: Some preliminary considerations concerning concentrations of oxygen in tissues. Bull. Math. Biophysics, 3:121, 1941.
31. Bloch, I.: Some theoretical considerations concerning the interchange of metabolites between capillaries and tissue. Bull. Math. Biophysics, 5:1, 1943.
32. Opitz, E., and Schneider, M.: Uber die Sauerstoffversorgung des Gehirns und den Mechanismus von Mangelwirkungen. Ergebnisse der Physiologie, biologischen Chemie und experimentellen Pharmakologie, *46*:126, 1950.
33. Schmidt, G. W.: A mathematical theory of capillary exchange as a function of tissue structure. Bull. Math. Biophysics, *14*:229, 1952.
34. Schmidt, G. W.: The time course of capillary exchange. Bull. Math. Biophysics, *15*:477, 1953.
35. Schmidt, G. W.: Determination of diffusion and permeability coefficients in nerve trunks. Bull. Math. Biophysics, *15*:489, 1953.
36. Landis, E. M.: Micro-injection studies of capillary permeability. III. The lack of oxygen on the permeability of the capillary wall to fluid and to the plasma proteins. Am. J. Physiol., 83:528, 1928.
37. Maurer, F. W.: The effects of decreased blood oxygen and increased blood carbon dioxide on the flow and composition of cervical and cardiac lymph. Am. J. Physiol., *131*:331, 1940.
38. O'Neill, J. F.: The effects on venous endothelium of the alteration in blood flow through the blood vessels in vein walls and the possible relation to thrombosis. Ann. Surg., *126*:270, 1947.
39. Wartman, W. B.: Factors other than cholesterol in arteriosclerosis. Minnesota Med., 38:749, 1955.

Surgical Correction of the Aorta Combined with Aortic Valve Regurgitation. J. M. Stallworth, M. D., Milton Weinberg, M. D., J. V. Jeffords, M. D. (Surgery 40:575-579, Sept. 1956)

A case history is presented of a 28 year old man with aortic insufficiency, coarctation of the aorta, and aneurysm of the descending aorta. These disorders were treated simultaneously by excision of the coarctation and aneurysm, with replacement of this segment of the aorta using a homograft and a Hufnagel aortic valve. The patient recovered satisfactorily and has returned to his usual full-time activities.

J. M. Stallworth

Complement-Fixation Titres in Tertiary Lymphogranuloma Venereum. A Study of Results After Treatment with Broad-Spectrum Antibiotics. Julius Goldberg and Leon Banov, Jr. British Journal of Venereal Diseases 32:37, 1956.

Patients with tertiary lymphogranuloma venereum continue to maintain circulating complement-fixation antibodies against the virus for as long as 27 months, even after clinically satisfactory antibiotic therapy. Diminishing complement-fixation titres cannot be used to establish a retrospective diagnosis of the disease even after clinically successful treatment with the broad-spectrum antibiotics.

Gracilis Muscle Transplant for correction of Urinary Incontinence in Male Children, Kenneth Pickrell, M. D., Nicholas Georgiade, M. D., Hugh Crawford, M. D., Carter Maguire, M. D., (Charleston) and Alex Boone, M. D. Ann. Surg. 143:764, June 1956.

This paper is directed primarily toward those patients with total incontinence resulting from the interruption of the nerve supply to the bladder, the perineum and its musculature. (Spina bifida and meningocele). The necessary preoperative studies and preparation are outlined and the actual operative technique is described and illustrated in detail.

The postoperative care and training of the patient are all important. A catheter is left in the bladder for 4 or 5 days after the operation and upon its removal, the patient becomes conscious of a new sensation of bladder fullness. Bearing down with the abdominal muscles produces a normal urinary stream, and complete bladder emptying. It is important to realize that the pressure caused by the reflex contraction of the bladder is not as great as the pressure in the bladder induced by voluntary contraction of the abdominal wall.

This operation has been performed on 6 male children, ranging from 5 to 9 years of age, who had been incontinent since birth because of spina bifida, menigocele or some neurogenic malformation involving the bladder and were classified as incurable and beyond salvage. Voluntary and controlled continence was established in each instance.

SURGICAL INTEREST IN FLUIDS AND ELECTROLYTES

1. POTASSIUM METABOLISM

LOUIE B. JENKINS, M. D.
Charleston, S. C.

In the past decade, knowledge concerning potassium metabolism has been garnered at a rapid rate. The acquisition of that information has awaited the development of productive tools. The recent appearance of the flame photometer as a commercially available instrument has provided accurate potassium determinations within a few hours, as compared with days for previous methods. Further, it is now possible to couple the flame photometer with the increasingly available and useful radioactive isotopes. These methods have firmly established the important role that potassium plays in physiologic and pathological states.

Another development in the field of electrolytes has been the increasing use of the system of equivalent weights. The increased emphasis on equivalents is justifiable since it is probably the more preferable system. An equivalent is that amount of ion that has the same electrical activity as 1 gram of hydrogen. A milliequivalent is one thousandth of an equivalent. The milliequivalent is generally used in electrolyte therapy due to the small amount of the ions encountered per liter of fluid. The surveyor relates all of his determinations of topography to a bench mark. It would seem equally desirable to connect all electrolytes to the "bench mark" of the hydrogen ion in order to express the activity of each as compared with the other electrolytes. As far as potassium is concerned, the amount in milligrams per 100 ml. is roughly 4 times the number of milliequivalents per liter. Such a factor allows easy transposition from either system to the other. Another easily remembered factor is that 40 mEq. of potassium is approximately 1.6 grams, which is the normal daily requirement of the ion.

The normal diet yields 70-125 mEq. of potassium per day.[1] Plant and animal cells have a high concentration of the ion. Foods such as meat, milk, orange juice and tomato juice are rich in the element. About 90% of the average of 100 mEq. of potassium ingested daily is absorbed proximal to the large bowel. The remaining 10mEq. is excreted in the feces. In a person in zero balance—that is, neither gaining nor losing weight—the 90 mEq. that is absorbed is excreted by the kidney. The total body potassium has been shown by radioactive isotope studies to be between 2300 and 4000 mEq. in the average 70 kilogram man. Intracellular potassium accounts for 98% of the body's potassium. Only 2% is in the serum or extracellular fluid. The serum level is normally 15-20 mgm. per 100 ml. (3.5-4.5 mEq./liter).

It is evident that the concentration of the ion in the cell is at least 20 times that of the extracellular fluid. It was formerly held that this difference was due to the fact that the cell membrane was practically inpervious to sodium and potassium and that interchange of the 2 substances did not occur. Radioactive potassium studies have produced conclusive evidence that movement of potassium across the cell membrane is an active process. For example, muscle cells lose potassium and acquire soduim during muscular activity. This movement is reversed during the muscular recovery phase. If the pH of the surrounding fluid is lowered, potassium will come out of the cell to neutralize the acid. The acid-base balance between the cells and the surrounding fluid is thus maintained by the emigration of potassium from the cell. The preservation of the difference between a low extracellular and a high intracellular level of the ion therefore involves an expenditure of energy.[6] This energy is probably provided by the metabolism of glucose.

Being the major intracellular cation, excessive loss or gain of potassium will produce cellular dysfunction that results in well established syndromes. The syndrome from ex-

cessive loss is much more frequently encountered by surgeons.

Excessive loss of potassium may occur from many sources. One such source is deprivation of food. Prolonged interference with food intake from anorexia, nausea, starvation, esophageal obstruction, etc. results in potassium depletion even in the absence of abnormal gastrointestinal losses. The failure to obtain the 30-40 mEq. of potassium that is required daily may produce potassium loss due to relatively poor renal conservation. Another factor of importance where there is lack of food is that cellular breakdown occurs in starvation, as well in such conditions as pyrexia and trauma. Destruction of the cell releases its potassium. The potassium of the destroyed cells is added to the extracellular fluid often at a rate that demands rapid excretion to prevent elevation of the serum potassium level. The potassium and nitrogen resulting from cell destruction are measurable in the urine. Normally there should be an average of 2.9 mEq. of potassium for every gram of nitrogen excreted in the urine as a result of cell breakdown.[8] These determinations are labeled the potassium:nitrogen (K:N) ratio. Such loss of potassium from cell destruction implies a lowering of the total body level of the cation.

The most common mechanism for the loss of potassium is the escape of gastrointestinal secretions. Martin and associates[2] found that 81% of their patients with potassium depletion had disease of the alimentary tract. Gamble[3] states that the total daily gastrointestinal secretion of potassium normally is about 66 mEq. (2.6 gm.). The loss of a liter of gastric juice by vomiting or by tube suction produces a loss of 10-15 mEq. of potassium. Gastric juice may contain as much as 40mEq. of potassium per liter. A liter of bile lost depletes the body of an average of 5 mEq. of the ion. Approximately the same amount is lost with a liter of pancreatic juice or of small bowel secretions. As much as 70 mEq. of the element may be excreted in a liter of diarrheal stool.[8] It is of interest that Bonsnes[5] has shown the loss of potassium in the stool and urine during the 3-5 day period of preoperative bowel preparation to be 100-300 mEq.

Another source of loss is the kidney. It appears that the kidney's function is designed more for the elimination of excess potassium than for the conservation of dwindling body potassium. The conservation of potassium definitely occurs, but it is relatively inefficient. The continuing excretion of potassium by the kidney in the presence of progressing depletion of the body's potassium occurs in the normal individual. After withdrawal of potassium from the diet, about 2 weeks is required for the urinary potassium to fall to the point of being level with the intake. In contrast, the kidney conserves sodium so efficiently that within 5 days after its elimination from the diet, the urine contains only a few mEq. of sodium.[4] The reduction of urinary potassium to a similar level of a few mEq. a day requires prolonged periods of potassium depletion or severe, acute deficits in disease states. These observations indicate that determinations of urinary potassium may be a good index of the severity of potassium depletion. Urinary potassium levels have been used by Roberts and her group[5] in the clinical handling of patients. If the urinary level is below 10mEq. with a daily volume of at least a liter, severe depletion is probably present.

The factors normally determining the rate of excretion of the ion by the kidney are obscure. It was formerly held that the serum potassium level may play the greatest role in determining potassium excretion. It is now suggested, however, that the intracellular level of potassium, probably in the renal tubule cells, is the deciding factor in regulating the rate of renal excretion.[4] The glomerular filtration rate of potassium in the kidney cannot play a significant part since about 1000 mEq. of potassium are filtered each day. Obviously, most of this must be reabsorbed. Reabsorption of about 90% of the filtered potassium occurs in the proximal tubule.[6] There may be more of the ion in the urine that is simultaneously being filtered at the glomerulus, particularly with overloading of potassium. Such evidence supports the concept of secretion of potassium by the cells in the distal tubules. Active secretion is apparently performed through the exchange of sodium ions in the filtrate for the

potassium ions in the cells. It appears that for the kidney to conserve sodium, it must lose potassium in exchange. Further support of this assertion is produced by the fact that the efficiency of the kidney to conserve potassium is augmented if sodium is restricted during the period of potassium withdrawal.[4] When the renal tubule cells have become depleted of potassium in prolonged withdrawal, apparently the hydrogen ion is substituted for potassium. Substitution of the hydrogen ion for the alkalizing potassium ion in the urine increases the acidity of the urine. The acidity is further augmented by the increased reabsorption in the renal tubule of filtered bicarbonate which is found in potassium depletion.[5] The appearance of an acid urine in potassium depletion has also proved to be a valuable guide in the clinical handling of patients.

Pathological changes in the kidney may produce variation from the normal pattern of excretion of potassium. Changes in excretion may lead to either excessive retention of potassium or to wasting of the element. Excessive retention of the ion is the more common and familiar. The main factor for its development is a reduction of the volume of urine below normal. Oliguria and anuria are essential for the development of an increased level of the cation in the extracellular fluid in the absence of oral or parenteral loading of the element. In anuria, the breakdown of cells will yield potassium to the extracellular fluid even if there is no intake of the substance. Lacking the route of renal excretion, potassium may accumulate in dangerous or even lethal quantities. Such accumulation may be seen in lower nephron nephrosis, terminal chronic glomerulonephritis and other forms of renal failure.

However, oliguria is not always productive of an increased extracellular potassium level. Newburgh has shown that certain diseased kidneys conserve potassium less efficiently than the normal kidney. The damaged kidney may be able to waste potassium if the damage to the tubules has been greater than the damage to the glomeruli. Wasting of potassium may lead to lowered serum levels of the ion. Such a situation is seen in renal tubular acidosis, Fanconi's syndrome (hyperaminoaciduria), the diuretic phase of acute renal insufficiency and primary aldosteronism.[4] Therefore, serum potassium determinations are necessary in renal disease before it is concluded that elevated serum levels of the ion are present due to diminished urinary output.

Other factors may produce changes in the normal pattern of excretion of the element. Prominent among these are the adrenal cortical hormones—cortisone, compound F, desoxycorticosterone and aldosterone. Their action is to increase potassium excretion. The increase is beyond the K:N ratio, indicating that it is not merely due to catabolism of tissues. The increased potassium excretion is probably a byproduct of the stimulus by the adrenal cortcal hormones to the kidney to conserve sodium. In order to conserve sodium from the glomerular filtrate, potassium must be expended by the renal tubule cells. Increased excretion of potassium caused by adrenal cortical hormones can be largely abolished by the rigid withdrawal of sodium. This probably occurs from the removal of the extra sodium from the tubular fluid which could be exchanged for potassium. A patient in the immediate postoperative period serves as an example of the interaction of these elements from the adrenal hormones. After an operation of moderate magnitude, potassium is excreted above the K:N ratio and sodium is retained for periods up to 5 days in the normal patient.[6] It would appear to be desirable to reduce sodium intake during this period to a level sufficient to replace extrarenal loss only. Such a reduction would prevent retention of excessive sodium which may produce edema and hypoproteinemia and increase the excretion of potassium.

Other drugs affect the renal excretion of the cation. Insulin was shown by Bendict to produce a decrease in serum potassium coincidental with a decrease in blood sugar. This decrease is apparently due to the deposition of potassium with glycogen in the cells of the muscle and liver. Epinephrin causes an initial rise and then a subsequent fall in serum potassium levels. Pitressin and dessicated thyroid raise the serum concentration of the ion. Testosterone produces a positive balance due to its anabolic effect.

The net result of the loss of the element in pathological conditions is to lower the total body potassium. The reduction of the serum potassium is practically always indicative of a total body deficit, but a normal serum potassium may be present where a cellular deficiency exists.

Hypopotassemia is productive of signs and symptoms arising from a cellular deficit of the element. These signs and symptoms show great individual variations and cannot be definitely correlated to the exact level of the serum potassium. The reduction of 1mEq. per liter of the ion may produce rather marked symptoms in one patient; twice that reduction may be symptomless in another instance. The rate of reduction is probably the important factor. The more rapid the rate, the earlier and more severe are the symptoms. The first complaint of the patient is usually weakness or excessive fatigue. In variable sequence, weakness is followed by apathy, abdominal distention, tachycardia and skeletal muscle paralyses. The abdominal distention is due to adynamic ileus caused probably by the rapid loss of intracellular potassium. It is apparently not related to the lowered serum potassium level. The intracellular deficiency explains why some patients continue in ileus some days after the serum potassium level has been restored to normal.[9]

A metabolic alkalosis due to hypopotassemia accompanies this clinical syndrome. In the post-operative patient this alkalosis commonly occurs on the fourth to seventh day. It is probably related to the shift of potassium back into the cells due to the lessening effect of the adrenal hormones. In hypopotassemic alkalosis, the plasma bicarbonate is increased, with a resultant increase in plasma pH. There is a decrease in urinary bicarbonate which is probably secondary to increased reabsorption of bicarbonate by the tubules. Increased reabsorption in the presence of an elevated plasma bicarbonate infers that potassium has an influence on the renal tubular mechanism concerned with bicarbonate.[4] The increased reabsorption of bicarbonate may be related to the increased use of the hydrogen ion by the renal tubule cell as the expendable element in the conservation of sodium when the tubular cellular potassium is lowered. This increased use of hydrogen ion is productive of an acid urine in the presence of plasma alkalosis ("paradoxic aciduria"). Hypopotassemic alkalosis is further augmented by the shift of sodium and hydrogen ions into the cells to replace the departed potassium. Usually sodium is replaced in one-half to two-thirds and hydrogen one-half to one-third of the amount of potassium which migrates from the cell. The shift of hydrogen into the cell results in a decrease in the extracellular acidity and is thereby additive to the plasma alkalosis.

The recognition of hypopotassemic alkalosis does not depend merely on the demonstration of a lowered serum potassium level. It has already been mentioned that the serum level may be normal when body potassium is low. Roberts and associates[5] point out that the diagnosis is proved better by the findings of a progressive plasma alkalosis with an acid urine, a lowered urinary potassium and a clinical situation in which potassium loss is occurring. The ECG changes of lengthened Q-T interval, depressed S-T segment and appearance of U waves may be of value where serum potassium levels are not available. The importance of detecting that hypopotassemia has been superimposed on chloride or sodium loss rests upon the fact that hypopotassemic alkalosis will not respond to the administration of sodium chloride. Potassium, either as a chloride or a phosphate, must be given to correct this salt-fast alkalosis.

The dosage of potassium to be used in any specific instance of deficiency is empirical. There is no completely reliable method to determine when the potassium defect has been repaired. If the oral route of administration is available, it is preferred. Potassium deficit is more quickly corrected by the ingestion of a full diet than by any other method. Liquids with high potassium content, such as tomato juice, milk or orange juice, may be used in a patient restricted to such foods. Additional potassium may be added to such liquids if necessary to regain a positive balance.

Parenteral therapy will be necessary if there is interference with oral intake. Potassium-free

fluids should not be administered longer than 3 days in any instance except when the serum potassium may be high. Vials of potassium chloride, available commercially in 40 mEq. doses, may be added to any infusion being administered without incompatibility. It is probably not wise to infuse more than 80 mEq. of potassium per liter of fluid nor more than 20 mEq. per hour of infusion. While hypodermoclysis is the safest route of administration, some patients complain of a severe burning sensation at the site, particularly with the larger doses. Therefore, intravenous administration is usually performed. Deficiencies of as much as 1000 mEq. (40 grams) may have to be repaired.

It must be remembered that several days of therapy are required to restore the deficit. Potassium should be given until symptoms have disappeared and the serum and urinary levels are in normal range. Thereafter, loss of potassium should be replaced volume for volume in so far as practicable from estimation or measurement. If the serum level is above normal in the presence of continuing loss, potassium should be withheld in order to avoid possible serious elevation of the potassium level. The cation should not be given in the first day after operation unless the serum level is known to be low. Neither should potassium be given in patients with low urinary output unless a low serum level is demonstrated. Patients who are acutely dehydrated should have potassium withheld until rehydration is well under way and adequate urinary output has reappeared.

If serum potassium determinations are not available in the management of patients in clinical situation where potassium loss may be present, other methods will be necessary. The ECG is used, but it is a much less reliable method of indicating potassium deficiency. Avoidance of potassium in patients who are acutely dehydrated, those who are immediately post-operative and those who are oliguric will prevent iatrogenic high serum potassium levels. The provision of at least 40 mEq. of the ion daily for the patient who has interference with food intake will replace the daily normal loss. Estimation of the amount of potassium in the loss of fluid from the gastrointestinal tract and replacement of the loss as it occurs will also help prophylactically against potassium depletion. If the syndrome has developed, the disappearance of an acid urine in an alkalotic patient and of the symptoms and signs of hypopotassemia indicate that the cellular deficit is well on the way to restitution. If oral intake can then be resumed, no further difficulty will be experienced.

Elevation of the serum potassium level is usually associated with blockage of renal excretion of the ion. The symptoms associated with an increased serum K level are remarkably similar to the symptoms of hypopotassemia. Muscular weakness is again the usual first complaint and paresthesias follow. The weakness may progress to flaccid paralysis of the extremities or trunk as the serum level is progressively elevated. The most important change in hyperpotassemia is disturbance of the conductive system of the heart. This change is best detected by the electrocardiogram. The ECG may show a progression from elevation of the T waves to ventricular standstill as the serum level of potassium rises.

Hyperpotassemia is a more serious situation that is more difficult to treat. At present, there are several modes of therapy that are useful. The best means available is the use of the artificial kidney. This instrument removes the excess potassium from the serum and corrects the acid-base balance. However, it is expensive and not generally available. Other means of removing the excessive cation have been perfusion of the alimentary tract with saline or sodium bicarbonate, lavage of the peritoneal cavity with the same solutions and use of cation exchange resins, although the latter produces unpredictable results.

Another means of combating elevation of the serum level is to produce sufficient calories to reduce tissue catabolism as much as possible. The daily introduction and utilization of 2000 calories from potassium free foods delays significantly the rise in serum potassium. If the oral route is not available, the provision of that many calories in the small amount of water given to oliguric patients demands the use of high concentrations of glucose, usually 50%.

Such solutions are highly sclerosive and are therefore given in the vena cava or right atrium. The concomitant use of insulin helps to prevent hyperglycemia and produces glycogen formation and storage. Insulin thus aids in reducing serum potassium, since glycogenesis carries potassium into the cells of glycogen-containing tissues.

The maintenance of a normal serum calcium by use of calcium gluconate is essential in hyperpotassemia. It is necessary since calcium has an antagonistic effect to potassium which is particularly important in the myocardium. The use of calcium as therapy for an elevated serum potassium has not shown much clinical value. The other serum electrolytes should be kept at normal values to avoid a possible aggravating effect on the hyperpotassemia.

The most effective way to resolve the problem of hyperpotassemia is to find a solution to the cause of the oliguria which produces it. Once adequate urinary output is reestablished, a high serum potassium is usually no longer a problem. If it cannot be reestablished, then the toxic effect of the increased serum potassium on the myocardium is a prominent factor in the patient's demise.

SUMMARY

1. The distribution and movement of potassium in the body are reviewed.
2. Excessive loss of potassium may occur from prolonged interference with food intake, from loss of gastrointestinal secretions and through the kidney due to relatively poor renal conservation.
3. The rate of excretion of potassium by the kidney is probably dependent on the level of potassium in the renal tubucle cells. These cells apparently secrete potassium into the renal tubular fluid in order to conserve sodium or other cation.
4. Pathological changes in the kidney may produce excessive retention or wasting of potassium.
5. The rate of excretion of potassium is affected by the adrenal hormones and various other drugs.
6. Excessive loss of potassium results in the well-established syndrome of hypopotassemia and manifests itself by weakness, apathy, abdominal distention, tachycardia and skeletal muscle paralyses.
7. The serum potassium level may be normal even when there is an intracellular deficit of potassium.
8. Hypopotassemia is accompanied by a metabolic alkalosis that is best diagnosed by a progressive plasma alkalosis with an acid urine, a lowered urinary potassium and a lowered serum potassium level.
9. Hypopotassemic alkalosis will not respond to sodium chloride alone, but requires potassium for correction.
10. Modes of therapy in hypopotassemia and hyperpotassemia are suggested.

REFERENCES

1. Levinson, B.: Potassium in Health and Disease. M. Times 83:33, 1955.
2. Martin, H. E., Reynolds, T. B., Snyder, E. N., Berne, C. J., Homann, R. E., Jr., Edmondson, H. A., Blatherwick, N., Fields, I., Wertman, M., and Westover, L.: Etiology and Treatment of Serum Potassium Deficits. J.A.M.A. 147: 24, 1951.
3. Gamble, J. L.: Chemical Anatomy, Physiology and Pathology of Extracellular Fluid. Harvard University Press, Cambridge, 1947.
4. Schwartz, W. B.: Potassium and the Kidney. New England J. Med. 253:601, 1955.
5. Roberts, K. E., Vanamee, P., Randall, H. T. and Walker, J. M.: Common Electrolyte Abnormalities Encountered in Bowel Surgery. S. Clin. North America, October 1955, p. 1189.
6. Sheppard, C. W.: New Developments in Potassium and Cell Physiology, 1940-1950. Science 114:85, 1951.
7. M & R Pediatric Research Conference No. 6: Potassium Metabolism. Sept., 1952.
8. Nadler, C. S.: Recent Advances in Potassium Metabolism. Am. J. M. Sc. 226: 88, 1953.
9. Moore, F. D. and Ball, M. R.: The Metabolic Response to Surgery. Charles C. Thomas, Springfield, 1952.
10. Schlesinger, B., Payne, W. and Black, J.: Potassium Metabolism in Gastroenteritis. Quart. J. Med. 24: 33, 1955.

AMMONIUM TOXICITY

KATHLEEN E. ROBERTS, PARKER VANAMEE, JOHN JACQUEZ, WALTER LAWRENCE, JR., AND J. WILLIAM POPPELL[*1,2,3]

Bollman and Mann[1] first demonstrated an elevated blood ammonium in hepatectomized dogs. It has been postulated that this abnormality may contribute in part to the high mortality in patients with liver failure. Since the liver is the major end organ for detoxification of endogenously or exogenously administered ammonium, this was indeed a logical assumption and has been confirmed by a large number of investigators on human patients. In 1943, Sapirstein[2] found that glutamate protected animals from ammonium-induced convulsions. These two separate findings have now been carried over to human subjects, and have provided the rationale for a better understanding and management of patients with hepatic coma. Our understanding of the effects of ammonium has been broadened by studies of the physiological alterations resulting from exogenously administered ammonium and a variety of experimental and clinical situations in which elevated blood ammonium plays a prominent part. It is evident that all patients with hepatic coma do not have an elevated blood ammonium, and the purpose of this paper is to discuss only those patients with liver disease who do have hepatic coma associated with an elevated blood ammonium. The experience of our group, as discussed here, is largely confined to patients with cirrhosis, bacterial infections, primary or metastatic cancer of the liver, chronic passive congestion of the liver due to heart failure, and temporary functional changes due to operative stress or anesthesia. Patients with acute hepatitis are few in our series, and in the ones who displayed an elevated blood ammonium, the treatment outlined here was frequently not effective in reversing the clinical course, even when supported with massive doses of cortisone.

Although ammonium is believed to be continuously formed as part of the overall metabolic processes associated with protein metabolism, in most organs it is immediately reincorporated into either amino acids, proteins or urea. There are certain organs, however, from which the measured blood ammonium is considerably higher in the venous blood than from the arterial blood supplying the organ. So efficient is the liver in the conversion of ammonium to urea, however, that excessive amounts do not normally accumulate in the peripheral blood. Under resting conditions, blood ammonium, as measured by currently accepted methods, is maintained at a concentration of less than 90-100 micrograms per 100 ml. and it is actually stated by some investigators that even this amount may be an artifact and the actual peripheral arterial ammonium may be negligible. In hepatic disease, however, the blood ammonium may rise to values as high as 700-800 micrograms per 100 ml., but more commonly an elevation to 300-400 micrograms is sufficient to result in symptoms and overt coma. There is no good correlation, however, between actual blood ammonium levels and the signs and symptoms displayed by the patients.

Ammonium may be released from exercising muscles, but is taken up by resting muscles. At rest, the major source of endogenously formed ammonium is the colon, and in the inferior mesenteric vein the ammonium concentration may be as much as twenty times that found in peripheral blood. Furthermore, it is increased by high protein feeding or by the presence of blood in the colon. The production of ammonium in the colon is the result of bacterial breakdown of urea and other

[1] From the Andre and Bella Meyer Physiology Laboratories, the departments of Medicine, Surgery and Chemotherapy of Memorial Center, New York, and the Cornell University College of Medicine, New York, N. Y.

[2] This work was supported by the Abbott Laboratories Fund, NCI Grant CS 9261, and NHI PH-1641.

[3] We are indebted to the following for the privilege of quoting their unpublished observations: F. Cuajunco, Jr., J. J. DeCosse, S. Dienst, G. Firmat, M. Hood, S. J. Horsley, Jr., T. McGraw, I. Nydick, N. Sager, A. E. Schwartz, G. Thompson, III, F. Wroblewski.

Paper presented at Greenwood, S. C.

nitrogenous substances, and the ammonium so formed is absorbed into the portal system. With good hepatic function the ammonium is largely detoxified and converted to urea. With hepatic dysfunction, either on the basis of temporary functional disturbances or pathological destruction, the ammonium formed in the colon is a major factor in elevating peripheral concentration. The basis for assuming that the major source of ammonium is from the kidney and colon is that eviscerated dogs have a negligible elevation in peripheral ammonium concentration, and intestinal antibiotics or cleansing enemas lower the intestinal formation of ammonium. In the three experiments summarized in Table 1, the inferior mesenteric vein ammonium decreased by an equivalent amount following 1) a tap water enema, 2) a soapsuds enema, or 3) neomycin. Similar results have been demonstrated with aureomycin.

TABLE 1

PROCEDURES	NH_4 CONCENTRATION Inferior Mesenteric Vein (micrograms per 100 ml.)	
	Before	After
Tap water edema	1395	286
Soap suds enema	2095	305
Intestinal antibiotic (Neomycin)	2202	209

The second major source of endogenous ammonium formation is the kidney. Nash and Benedict[3] showed that the ammonium formed by the kidney may diffuse into the renal vein as well as into the urine. This has been confirmed, and although its formation is greater in metabolic acidosis, the renal formation of ammonium is a continuous process, even in alkalosis. Quantitatively, the amount of renally formed ammonium which diffuses into the renal vein and thus enters the systemic circulation, is between 15-45 microEq./min. in dogs, or a total of up to 65mEq./day. In human subjects, the renal formation of ammonium may be 2-3 times this amount.

There is a gradation in ammonium content at various sites when the blood ammonium is elevated, but only at two sites when the blood ammonium is normal. As shown in one experiment in Table 2, the pulmonary arterial ammonium was 140 micrograms per 100 ml. when the peripheral arterial ammonium was only 101 micrograms. Although this is a very small difference, and one that may not be thought significant, its consistency warrants attention. Note, however, that there is normally no gradient between peripheral arterial and venous ammonium. In situations attended by an elevated blood ammonium content, however, the peripheral arteriovenous difference may be marked. As is shown in the lower part of Table 2, there is a marked difference between the peripheral arterial ammonium, which is approximately 50% of that in the pulmonary artery, and the femoral venous blood, which is almost a quarter of that in the femoral artery. It has also been shown that there is a similar difference in peripheral arterial and venous concentrations of ammonium in patients who have elevated blood ammonium. Arterial ammonium content may be as much as twice that measured in a simultaneously drawn venous sample in human subjects with ammonium toxicity. Worthy of mention also is the finding that there is a wide A-V pH and CO_2 difference in patients with ammonium toxicity and respiratory alkalosis.

TABLE 2

BLOOD AMMONIUM CONCENTRATION
Micrograms per 100 ml.

	Pulmonary Artery	Femoral Artery	Femoral Vein
Normal Dog	140	101	100
Dog with Elevated Blood Ammonium	801	401	111

The observation that there is a gradient of ammonium between pulmonary artery, peripheral artery and peripheral vein implies that ammonium diffuses into, or is taken up by tissue. This does not deny, of course, that ammonium may disappear by other means, such as changes in hemoglobin absorption, or losses across the alveoli. In fact, Poppell and Jacquez[4] have found ammonia in significant amounts in the expired alveolar air in normal

subjects. Arterial sampling may be more ideal for diagnostic purposes, but it is probably the venous ammonium which is in equilibrium with the tissues. The diagnosis of ammonium toxicity should not be compromised if arterial blood is not available, since in the majority of patients studied by us venous blood samples were usually elevated sufficiently to confirm the diagnosis.

In our experience, the common neurological changes in patients with ammonium toxicity consist of: 1) unilateral or bilateral Babinski reflexes, 2) painful plantars, 3) flapping tremor, and 4) clonus. Initially, the patients may have only confused mentality and slurring of speech, which progresses to loss of memory and, eventually, coma. The most characteristic feature of the neurological changes is their transient and shifting nature. Although convulsions and vomiting are a common feature in dogs given any type of ammonium salts, this is an uncommon finding in patients with elevated blood ammonium. The cause of the neurological changes has not been clarified, but the decreased cerebral oxygen consumption which has been demonstrated by Wechsler and his group[5] may well be significant. It is entirely possible that the neurological changes are enhanced by the respiratory alkalosis which so frequently accompanies ammonium toxicity. In addition, there is known to be a direct action of ammonium on nervous tissue.

The most common electrolyte alteration we have encountered in association with ammonium toxicity is a respiratory alkalosis which is characterized by an elevated pH and a normal or decreased carbon dioxide content of the plasma. This finding correlates well with the often observed clinical finding of hyperventilation which accompanies ammonium toxicity. The degree of hyperventilation and the severity of the respiratory alkalosis show no correlation with the degree of elevation of blood ammonium when it reaches a critical value of 160 micrograms or more. The three patients shown in Table 3 had elevated blood ammonium levels which ranged between 166 and 315 micrograms, and yet the blood pH in all three patients was 7.5-7.54,

TABLE 3

Pt.	Carbon Dioxide mM/L	K	pH	pCO_2	Bl. NH_3 ygm/%
1	25	5.5	7.50	32	166
2	25	3.55	7.50	32	267
3	26	4.5	7.54	30	315

and total carbon dioxide content was 25-26 mM/L. with a plasma pCO_2 of 30-32 mm. Hg.

The mechanism leading to respiratory alkalosis in association with ammonium toxicity is not understood, but the hyperventilation which is commonly observed in patients suggests that ammonium is either a direct or indirect respiratory stimulant. Furthermore, it is possible to show in dogs that respiration is stimulated sufficiently to cause a respiratory alkalosis whenever neutral salts of ammonium, such as ammonium acetate, are infused intravenously. This is illustrated in Figure 1, which shows a series of dogs who were infused with ammonium acetate and displayed increased pulmonary ventilation sufficient to cause respiratory alkalosis. The open circles show the blood pH in the upper part of the figure, and the pCO_2 in the lower part of the figure, in dogs during the control peroid. The closed circles illustrate the pH and pCO_2 following the infusion of ammonium acetate. As shown

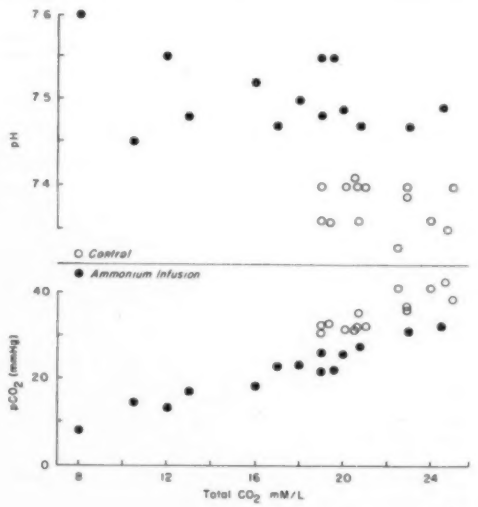


Figure 1

here, all animals increased their pH and decreased their pCO_2 following the ammonium infusion.

Earlier, we suggested that ammonium may stimulate respiration either by impaired oxygen unloading or changes in cardiac output, or both. This was based on two observations: 1) that of Wechsler, *et al*,[5] who had shown decreased cerebral oxygen consumption, and 2) our finding of terminal electrocardiographic changes with ammonium infusion which resembled those occurring with hyperkalemia and acidosis. Therefore, experiments were carried out to determine total body oxygen consumption and cardiac output in dogs infused with ammonium acetate. The results, shown in Table 4, were the opposite

TABLE 4

	0_2 Consumption cc/min.	Cardiac Output L/min.	Pulmonary Ventilation L/min.
CONTROL	114	1.58	2.4
INFUSE NH_4 ACETATE →			
	170	2.45	12.1

of what we anticipated. Indeed, it was noted in the majority of dogs, that cardiac output and oxygen consumption were actually increased. Moreover, it was easily demonstrable that peripheral utilization of oxygen and the A-V oxygen difference were both much increased. This clearly, therefore, was not the mechanism whereby ammonium increased ventilation. Experiments carried out by Lawrence and Schwartz[6] have shown that there is no direct effect of ammonium on the carotid body or aortic chemoreceptors. Therefore, they postulate that the respiratory alkalosis associated with ammonium toxicity is probably due to stimualtion of the respiratory center itself.

In addition to respiratory alkalosis, other associated alterations which may be found with ammonium toxicity include elevation of lactic acid, hypokalemia, and frequently hypo phosphatemia. Alterations in glucose metabolism and acetonuria have been observed. Terminally, the respiratory alkalosis found in connection with ammonium toxicity, like the respiratory alkalosis occasioned by other causes, may progress to metabolic acidosis.

Amino acid hydrolysates not only contribute to increased metabolic formation of ammonium, but these intravenous fluids have a high ammonium content which may range up to 20,000 micrograms per 100 ml. Therefore, this source of ammonium should be recognized. Stored blood has been found to have a slightly elevated ammonium content, and it is not uncommon for patients with poor liver function and gastro-intestinal bleeding, who are given massive transfusions, to go into hepatic coma. In these patients it is probable that the blood in the gastrointestinal tract contributes as much as the transfused blood, since the former provides an excellent medium for bacterial decomposition. In addition, massive hemorrhage decreases hepatic blood flow, which would further contribute to ammonium toxicity. The current use of commercial carbonic anhydrase inhibitors, such as Diamox, may result in an elevation of blood ammonium if hepatic function is severely compromised. It is not uncommon to observe mild and transitory elevations of blood ammonium in a variety of clinical situations not associated with detectable pathological or biochemical evidence of hepatic disease.

Occasionally, the post-operative patient may display an elevation of blood ammonium which has no apparent cause and is usually transient in nature. The decrease in hepatic function which has been described during operative stress and anesthesia may be a contributing factor in this group of patients.

There is often a slight elevation of blood ammonium in metabolic acidosis which may possibly contribute as a respiratory stimulant. It is of interest that the elevation of blood ammonium that has been noted in metabolic acidosis usually does not cause such severe signs and symptoms as those observed in patients with an elevated blood ammonium associated with respiratory alkalosis. In fact, a majority of the patients with acidosis and elevation of blood ammonium displayed no detectable symptomatology until blood ammonium levels were markedly elevated. In

patients with an elevated blood ammonium, the clinical signs of ammonium toxicity are more prominent in febrile than in afebrile patients. Furthermore, the tolerance to ammonium is greater in animals made acidotic either by respiratory or metabolic means. The finding that an elevated blood ammonium associated with an increase of temperature and respiratory alkalosis usually produced more clinical deterioration in animals and humans led to the suggestion by Jacquez[7] that the partial pressure of ammonia (pNH_3) is probably the relevant factor in producing toxicity. According to his calculations, the pNH_3 would be greater with an alkaline pH and an elevation of temperature. If his assmption is correct, as the evidence indicates, measurements of plasma pHN_3 are probably more compatible with comparative clinical symptoms and may give a more sensitive biochemical index to the clinical status of a patient.

In human subjects and dogs, Lawrence and Schwartz[6] have defined elevation of peripheral blood ammonium to values as high as 300 micrograms per 100 ml. immediately following muscular exercise. This elevation is usually accompanied by a combined respiratory and metabolic acidosis which probably protects the exercising subject from severe symptoms of ammonium toxicity. The physiological importance of such elevations in muscular exercise has not been clarified, but it is probable that there is a contribution by ammonium to the increased minute respiratory volume, increased cardiac output and oxygen utilization which has been observed in muscular exercise. These investigators have also described a similar elevation of blood ammonium following electroshock convulsions. Blood ammonium levels may increase in hemorrhagic shock to levels as great as 800 micrograms, and a correlation between the elevation of blood ammonium and irreversibility of hemorrhagic shock in dogs has been found by Horsley *et al.*[8] Although respiratory alkalosis is a common finding in patients with ammonium toxicity, a blood ammonium level elevation is not always accompanied by respiratory alkalosis in experimental situations. Thus, in hemorrhagic shock, total hepatectomy in dogs, and muscular exercise, there is always an acidosis. On the other hand, all the situations associated with an elevation of ammonium are accompanied by a marked increase in respiratory minute volume.

Therapy of Mild Ammonium Toxicity

In patients whose blood ammonium is not markedly elevated and liver function not seriously impaired, the situation is easily reversed by conservative therapy, such as protein restriction, the use of intestinal antibiotics and the removal of precipitating factors such as ammonium exchange resins, Diamox and ammonium salts. The most important approach in these patients is the removal of precipitating factors and a high carbohydrate regimen (i.e., up to 300 grams/day), along with cleansing enemas (or intestinal antibiotics) and vitamins. Furthermore, spontaneous regression of ammonium toxicity is not uncommon in this group of patients, even with no specific therapy. If, as suggested by Jacquez,[7] a temperature elevation increases the pNH_3 and thus the toxicity of ammonium, then it is important to lower the temperature of the patient by treating any infectious process which may be present.

If the ammonium toxicity is severe and the patient is in a deep unresponsive coma, more vigorous therapy may be required. The essentials of therapy under these circumstances may be outlined as follows. Administer glutamate in doses up to 80-120 grams by vein as the monsodium and monopotassium salt. If the potassium salt is given, its concentration should not exceed 40mEq./L. of potassium, and the remainder should be given as the sodium salt. If heart failure is present, the glutamate may be given by mouth or stomach tube as glutamic acid. Although the dosage outlined here may seem excessively high, we have met with no success with the usual recommended dosage of 20-25 grams. In patients with esophagitis and esophageal varices, glutamic acid should be administered with great caution, or it should be administered as the potassium salt together with antacid therapy to decrease the deleterious effects of increased acidity on the esophageal mucosa.

Sodium glutamate therapy may be followed by the development of metabolic alkalosis and hypokalemia. Both are easily corrected by the

administration of potassium salts in a dosage of 80-100 mEq./day for four to five days, providing of course, that renal function is adequate. If part of the glutamate is given as the potassium salt, this would of course minimize the hypokalemia. The mechanism of metabolic alkalosis following sodium glutamate therapy, and the mechanism whereby the elevated blood ammonium is lowered is said to be on the basis of glutamate combining with ammonium to form the metabolizable glutamine. The sodium administered with the glutamate is then available to combine with metabolically available carbon dioxide to form sodium bicarbonate. Although the chemical alkalosis following sodium glutamate therapy is often quite severe, the clinical symptomatology is unremarkable, and usually no overt findings can be demonstrated. The complication of metabolic alkalosis does not, of course, occur when glutamic acid is administered orally since no sodium is available to form bicarbonate bound base.

Lawrence, Dienst and McGraw[9] have lowered blood ammonium in dogs with alpha-ketoglutarate, which presumably has an effect similar to that of glutamate, in that it combines with ammonium to form glutamine. However, this therapy has not been tried in human subjects. Of interest also is the observation of Wrobleski and Nydick[10] that elevation of transaminase (serum glutamic-oxylacetic transaminase), which has often been reported in acute hepatic necrosis, may be lowered by the administration of glutamate. This finding cautions against unwarranted optimism regarding patients with hepatic necrosis whose transaminase drops after glutamate therapy, since a drop in transaminase after treatment with glutamate may be an artifact due solely to glutamate administration rather than improvement or cessation of the necrotic process.

Removal of precipitating factors and cleansing enemas, or administration of intestinal antibiotics, are important aspects of therapy, as outlined earlier. Restriction of protein, which is often necessary in severe ammonium toxicity, may conflict with the obvious need of protein for regeneration of liver tissue. In these cases it has been our practice to restrict protein only until coma and ammonium toxicity have been controlled, and to reinstitute protein in 20 gram increments at 4 to 5 day intervals, as tolerated. If necessary, oral administration of glutamate in a dosage of 20 to 40 grams a day, when given as a prophylactic measure, may prevent coma when the protein is increased. In post-operative patients with low plasma protein salt-poor albumin is given in a dosage of 25 grams per day.

Correction of abnormal electrolytes in the plasma may be accomplished as indicated. If potassium or phosphate are low, these electrolytes should be administered, along with supportive and adequate amounts of glucose and vitamins. Respiratory alkalosis may be corrected with 10% CO_2 by nasal catheter or tent. This concentration of carbon dioxide by face mask, however, is not tolerated by patients, and 5% CO_2 by nasal catheter or tent is insufficient for correction of the respiratory alkalosis. Actually, the respiratory alkalosis need not be treated unless severe, if the blood ammonium is lowered by other means, since the stimulus to respiration is thereby removed. A high carbohydrate diet and limitation of sedatives are obvious necessities in the therapy of ammonium toxicity.

Increased tracheal secretions are an important hazard of hepatic coma and can be dealt with only by adequate naso-tracheal suction. Aspiration pneumonia, bleeding varices, and respiratory complications are frequently associated with hepatic coma and contribute to the high mortality. In patients with superimposed pulmonary complications and anoxia, the therapy outlined here has failed in the majority of cases treated by us.

Summary

The clinical and biochemical findings of ammonium toxicity have been outlined and a therapeutic regimen has been suggested. The evaluation of any therapeutic regimen should be tempered by the realization that spontaneous recovery is not uncommon in hepatic coma, and that all cases of hepatic coma may not be entirely due to an elevated blood ammonium. Nevertheless, the regimen outlined has afforded a better measure of success than has previously been achieved.

REFERENCES

1. Bollman, J. L. and Mann, F. C.: Studies on the physiology of the liver. XVIII. Effect of removal of the liver on the formation of ammonia. Am. J. Physiol. 92:92, 1930.
2. Sapirstein, M. R.: Effect of glutamic acid on central action of ammonium ion. Proc. Soc. Exper. Biol. & Med. 52:334, 1943.
3. Nash, T. P., Jr., and Benedict, S. R.: The ammonia content of the blood, and its bearing on the mechanism of acid neutralization in the animal organism. J. Biol. Chem. 48:463, 1921.
4. Poppell, J. W. and Jacquez, J.: Unpublished observations.
5. Wechsler, R. L., Crum, W. and Roth, J. L. A.: The blood flow and O_2 consumption of the human brain in hepatic coma. Clin. Research Proc. 2:74, 1954.
6. Lawrence, W., Jr. and Schwartz, A. E.: Unpublished observations.
7. Jacquez, J.: Unpublished observations.
8. Horsley, S. J., DeCosse, J., Hood, M., Sager, N., Roberts, K. E. and Randall H. T.: Elevation of blood ammonium in hemorrhagic shock. Submitted for publication.
9. Lawrence, W., Jr., Dienst, S., McGraw, T.: Unpublished observations.
10. Wrobleski, F. and Nydick, I.: Unpublished observations.

MEDICAL COLLEGE CLINICS

THE MEDICAL COLLEGE OF SOUTH CAROLINA

ELECTROCARDIOGRAM OF THE MONTH

THE VECTORCARDIOGRAM

JOHN A. BOONE, M. D.
Charleston, S. C.

From the Dept. of Medicine.

In the past few years a new variant of electrocardiography has arisen to plague the average practicing physician, who has had trouble enough keeping up with refinements and developments in ordinary electrocardiography. In its simplest terms, a vectocardiogram can be regarded as really another way of recording an electrocardiogram, although we have grown so accustomed to the ordinary way of recording them that the new method appears superficially more complex and strange.

An ordinary, or "scalar" electrocardiogram is a graph of the variation of cardiac voltage plotted against time, with each lead of the cardiogram "looking at" the heart from a different angle. A vectorcardiogram can be constructed from any two electrocardiographic leads by plotting them against each other on polar coordinate paper. The resulting picture is that each heartbeat traces a loop, where any point on the loop represents the size and *direction* of the average electrical voltage of the heart at that instant. It is in other words, a graph of the variation in size and direction of the average, or "vector" voltage of the heart during each cycle of heart beat. If the proper leads are used, all scalar electrocardiographic leads in a given plane can be deduced and reconstructed with fair accuracy from a single vector loop, since all the information needed is present in the loop.

The limb leads of an ordinary electrocardiogram actually represent the voltages in the frontal plane of the heart. If we use two of them to construct our vectorcardiogram, we obtain the "frontal spatial vectorcardiogram". The chest leads in an ordinary electrocardiogram represent the voltages in the horizontal plane of the heart, as we look down at the top of the patient's head from above. If we use two of these to construct our vectorcardiogram, we obtain the "horizontal spatial vectorcardiogram". In a similar way, we may construct a "sagittal spatial vectorcardiogram" if we use two esophageal leads to plot it, and obtain a

[While interpretation of the electrocardiogram has made great strides since Einthoven's day, the technical quality of the recordings has undergone remarkably little change. Tracings are recorded more conveniently on our modern direct-writing oscillographs but they are actually less accurate representations of the heart's electrical activity than those made on the old string galvanometer by Einthoven in the early 1900s.

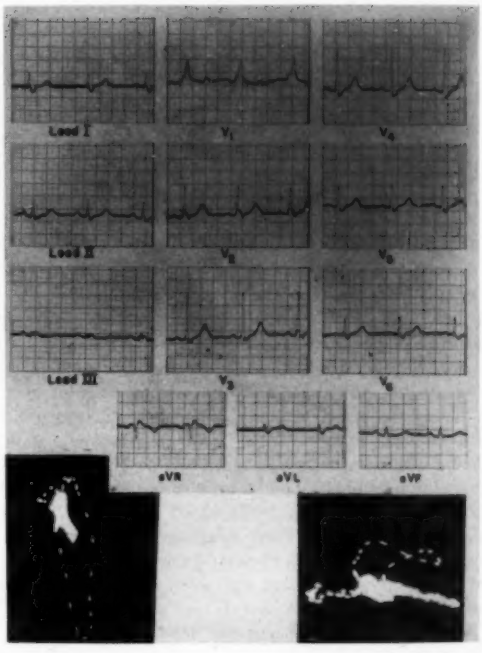
Dr. Boone contributes this month's discussion illustrating one of the newer recording methods of special interest in electrocardiographic research. — Dale Groom, M. D.]

picture of the heart voltages looking at the heart from the patient's side.

Instead of laboriously plotting vectorcardiograms from scalar electrocardiograms, they can be quickly obtained on the face of a cathode-ray oscilloscope if we connect the two electrode terminals of one electrocardiographic lead to the horizontal axis of the oscilloscope, and those of another lead to the vertical axis. The loop formed on the face of the oscilloscope can be photographed for record purposes. Another advantage of the oscilloscope method is that the beam of the cathode-ray tube may be interrupted at any convenient rate, and the loop is traced as a series of dashes, each representing a fixed interval of time, so that the exact timing of various portions of the loop in the cardiac cycle are recorded.

The relative usefulness of vectorcardiography versus ordinary electrocardiograms is still a matter of some debate among cardiologists. There is one situation at least, however, where vectorcardiograms made with the oscilloscope and using timing markers by beam interruption appear to have definite advantage over the usual electrocardiogram. The differentiation between right bundle branch block and marked right ventricular hypertrophy is not easily made by the electrocardiogram but each of these abnormalities has a clear-cut pattern of its own by vectorcardiogram.

The illustrations show an example of how this differentiation is made. The electrocardiogram shown has all the characteristics of right bundle branch block. However, in right ventricular hypertrophy, (lower left) a large smooth vector loop will show the right ventricle to be contracting in normal time sequence, the wide spacing of the time markers indicating no localized delay in the formation of the ventricular pattern. For comparison is shown on the right the characteristic vector loop of right bundle branch block, where the left ventricular loop is first formed, and then the loop of closely spaced, slowly moving time markers forming a "tail" over the right ventricle and beginning after the left ventricular loop is completed.



SUPINE HYPOTENSIVE SYNDROME

A CASE REPORT

EDWARD J. DENNIS, M. D.
Department of Obstetrics and Gynecology

M. J., a 20 year old prima-gravida was seen on the 25th of April, 1956 for admission examination to the Florence Crittenton Home and Hospital in Charleston. Her last normal menstrual period began December 7, 1955 and she had had no complications prior to the date of this examination.

Physical examination revealed a well developed and nourished white female in no distress. Her weight was 161 pounds and her blood pressure was 110/80 mm. of mercury in both arms. Complete physical examination was entirely normal and the uterus was found to be enlarged to the size of a 20 weeks gestation.

Laboratory studies on this date showed a hemoglobin of 12.5 grams with a normal red count and

differential. The blood type was type 4 (O) Rh positive and serum tests for syphilis were negative.

Her antenatal course was entirely normal with a total weight gain during pregnancy of 20 pounds. Her blood pressure at the time of her initial visit was 110/80 and subsequent recordings were all within the range of 100 to 110 systolic and a diastolic of 60 to 80 mm. of mercury.

At 2 A. M. on September 23, 1956, labor began spontaneously at 41 weeks gestation. Rectal examination at that time revealed the cervix to be fully effaced, 3 cm. dilated with the vertex presenting in left occipital anterior position at station plus 1.

At 11:45 A. M. rectal examination revealed the cervix to be fully dilated with the vertex on the perineum. The patient was placed in the lithotomy position in preparation for delivery. Within a matter of 3 minutes she began to complain of difficulty in catching her breath and of being cold. Her face was pale and a check on her pulse and blood pressure revealed a pulse rate of 140 per minute and blood pressure 60/20 mm. of mercury. The fetal heart tones were present in the right lower quadrant at a rate of 38 per minute. The patient was immediately taken out of the lithotomy position and allowed to turn on her side, following which her blood pressure rose immediately to 120/80 and the fetal heart tones increased to a rate of 120 per minute.

In the absence of any signs of uterine rupture or other intraabdominal catastrophe and the fact that the patient responded to being changed from the supine to the lateral position, it was felt that this was almost certainly a manifestation of the supine hypotensive syndrome and that she could be better cared for at a fully equipped hospital.

Thus, she was transferred to the Medical College Hospital, the anesthesiology department having been notified that she was to be admitted and the conditions that existed. She was taken immediately to the delivery room and an ampoule of neosynephrine diluted in 500 ml. of glucose in water was started in an intravenous drip. She was again placed in the lithotomy position and even with the neosynephrine solution running at a rate of 40 to 50 drops per minute, the blood pressure again dropped to 60 systolic and the fetal distress was again manifest by a tremendous drop in the fetal heart rate. After having received the solution for a period of 5 minutes and at a drip approximating 100 to 120 per minute, she was placed on her back and under pudendal block and inhalation of nitrous oxide and oxygen, she had a low forceps delivery of a 7 pound, 12 ounce male infant in good condition. Immediately after delivery, the intravenous infusion of neosynephrine was stopped and her blood pressure remained stabilized at 110/70. The fetus showed no evidence of any abnormality.

Exploration of the uterus with manual removal of the placenta showed no evidence of uterine rupture and there were no cervical lacerations. The episiotomy was repaired without difficulty and the total amount of blood loss at the time of delivery was estimated to be 100 ml.

Discussion

This patient presents a syndrome frequently recognized by all of us doing obstetrics, but it is unusual in that it occurred during labor. Many of us have seen women in the last trimester visit the clinic, or office and present the picture of peripheral circulatory collapse while lying on the examining table, or, state that they have found it much more comfortable to lie or sleep on their sides than on their back during the later stages of pregnancy.

Howard *et al* reported in 1952, that of 160 term pregnant women seen consecutively they were able to detect the syndrome in 18 women, or in 11.2%. This high percentage may be explained by the fact that the patients were made to lie on their back for a period of 3 to 7 minutes in order to elicit the syndrome. Their criterion for including a patient in this category was a depression of systolic pressure of 30 mm. of Hg. or an observed pressure of 80 mm. or less.

The theories as to the etiology of this condition are divided between (1) stimulation of sensory pathways in the abdomen by weight of the uterus, and (2) pooling of blood in the lower extremities because of the uterus pressing on the inferior vena cava. Ligation of the inferior vena cava in pregnant dogs produced a marked fall in blood pressure, while in the non-pregnant dog, there was no change. In pregnant women, cannulization of the femoral vein at the level of the femoral triangle and placing the pregnant women in a supine position produced a significant rise in venous pressure. This was not true in the lateral or other positions, nor was it true in non-pregnant women. At cesarean section, the increase in femoral vein pressure in the supine position was relieved by elevating the uterus from the vena cava.

The clinical aspects may be summarized as follows:

1. It seems to occur only in late pregnancy.
2. It is relieved by turning to either side or by standing erect.
3. It is cured by delivery.
4. Full development requires at least 3 to 7 minutes.
5. It is not clinically recognizable during labor.
6. Varicose veins are noticeably more distended when the syndrome is present.
7. Deep inspiration partially relieves the blood pressure depression.

The case presented varies the usual clinical picture in revealing that the syndrome can occur during labor. A knowledge of its existence and probable cause is essential when one considers that it may closely mimic the dreaded catastrophe of rupture of the uterus during labor. In fact, Howard and Mengert[1] report a case in which an immediate laporotomy was done with a preoperative diagnosis of rupture of the uterus only to realize too late the cause of the peri-

pheral circulatory collapse as being the supine hypotensive syndrome.

REFERENCES
1. Howard, Ben K. et al Ob-Gyn 371, Vol. 1, 1953.

PRESIDENT'S PAGE

Recently in the Charleston papers there appeared a charge by a state representative that collusion between "certain legal firms and unethical doctors" is responsible for higher insurance rates in Charleston. Dr. Robert Wilson, Secretary of the South Carolina Medical Association, in a published letter, stated that the Association maintains a Mediation Committee for the thorough investigation of such charges. Dr. Richard Hanckel stated that the Charleston County Medical Society, of which he is President, is prepared to investigate any specific charges presented to it. The officers of the Charleston County Bar Association made a statement to the same effect with regard to the legal profession. An editorial in the *News and Courier*, while recognizing the value of such investigations, states that "basically, the problem stems from the fact that under existing South Carolina law there is no way for a defendant in an automobile accident case to have the plaintiff examined by another doctor." It further states that federal courts, recognizing the necessity, make provision for another physician to examine the plaintiff, and that in New York State a recent law provides for a panel of physicians nominated by medical societies.

Investigations by professional committees are in order and should be made particularly for the purpose of maintaining standards of conduct. While they would be helpful they would probably be inadequate to control such situations. Professional censure would not be much of a deterrant to the type of physician who would give false testimony. To have his license taken away would likely require an involved court procedure. In Charleston, recently, it was only after concerted and prolonged effort that an abortionist was proven guilty. It would appear that the solution to the problem would be a change in the South Carolina law. The physicians of the State should work toward this end.

William H. Prioleau, President
S. C. Medical Association

November 28, 1956

Editorials

OLD AGE, A SERVICE CONNECTED DISABILITY

If we read this quotation correctly, there is no promise of a reduction of the unjustified overactivity of the Veterans Administration.

"Military Surgeons Hear Reports From Government Agencies.

Officials of federal agencies dealing in medical matters made reports of their activities at the 63rd annual meeting of the Association of Military Surgeons of the U. S. Delegates from 30 countries attended the 3-day sessions. Dr. Roy Wolford, deputy chief medical director of the Veterans Administration, told of the agency's increasing role in treating aging veterans with chronic diseases and disabilities. 'Nowhere else in the world are found patients in all stages of these diseases in such large numbers or under conditions so suitable for clinical investigation as in Veterans Administration hospitals,' he said." (*AMA Wash. Letter*)

Well, it must be a comfort to the veteran, if he can't see beyond his own nose. The next step may be to have the VA cover deliveries and the ailments of childhood, since every child is likely to be a future veteran, and should be in the best of condition to develop the disability for which he will receive life long treatment.

ONCE MORE THE POLIO VACCINE

Public health officials are advocating strenuously that we taxpayers contribute another 30 million dollars to supply free polio vaccine to all comers. No doubt the practitioner will again be expected to donate his time and services, and to continue to administer vaccine at the bargain rates which he has established.

In light of recent experience, one cannot question the virtue of general vaccination, but one may question the desirability of perpetuating the present approach. Vaccine has gone begging in the face of an apathetic public, private physicians have given large quantities of the available supply at a fee which scarcely compensates for their trouble and equipment and especially for the involved record-keeping which is required and which might now well be abolished.

Perhaps it is time to put polio vaccine in the same category as other vaccines, to let the public health people do the converting and the urging in a bigger way, even if it costs money, and to confine the distributing of "free" vaccine to those who cannot afford to go to their physicians. Perhaps this is an idea too old fashioned to appeal to the present generation.

COMMUNITY AND OTHER FUND CAMPAIGNS

The Journal has pointed out before that the contributions in cash of the medical profession are not usually pleasantly comparable to those of some other groups in the community. Many physicians feel that they donate in many other ways to the welfare of the community, and of this there is no question, but the fact remains that the physician should also have sufficient regard for the efforts of the people who afford him a livelihood to make his just contribution to those funds which support their worthy efforts.

The activities which these funds support are all well known, well documented, and well budgeted, so that a contributor knows with some degree of accuracy where the money which he contributes is to go and what it should do. It is somewhat questionable whether the same thought applies to some of the individual funds, which seem to have no end. We are accustomed to thinking in terms of giving to The Polio Foundation, to The Tuberculosis Association, and to other well known organizations which do not participate in the general fund-raising campaigns. Unfortunately, there has arisen a multitude of funds each devoted to some very specific disease or purpose, and it seems rather doubtful that their independent existence can be completely justified, especially as some of the other

well-established foundations include in their programs the care or investigation of many of these particular conditions. Public interest generally centers around some cases or a few cases in a community which by the nature of their affliction draw large public sympathy. Perhaps the example of the Polio Foundation, which after long last has perhaps justified its other tremendous expenditures by promoting the work on polio vaccine, encourages the thought that simply by raising a sum of money and placing it in the hands of investigators any disease in question may be conquered This is a doubtful supposition, and one is inclined to think that where money is free and easy, investigation may be developed to suit the purse. One also wonders whether it might not be a better arrangement to project a research project, estimate the budgetary arrangement, and then set a goal for raising a certain sum of money, rather than doing as is now done in a reverse way. Duplication and reduplication of effort and fine division of public interest and public contribution may cause ultimate defeat of the very purposes of the many campaigns which beckon to contributors.

FOUNDATION FOR EYE CARE

At the recent meeting of the American Academy of Ophthalmology and Otolaryngology in Chicago there was created a new organization, which is called The Nationel Medical Foundation for Eye Care, the purposes of which are set forth in an article which appears elsewhere in this Journal.

For some time it has been felt that our magnificent Societies which are devoted to scientific and educational features lacked organization to act as a body when certain functions seemed necessary. Ophthalmology has been attacked, and the field invaded by optometrists, who are, in finality, endeavoring to practice medicine. They have made this effort in several states, and are trying to gain by legislation that which they lack in knowledge gained from years of preparation and education. Moreover, they have attempted to limit the ancillary services aligned with ophthalmology. The situation is more serious than it appears on the surface.

The National Medical Foundation for Eye Care, by its aims and efforts, will inform the public adequately about the cults, and will serve to coordinate all the various medical groups interested in demanding that our people have the best eye care in the world. It is hoped that all physicians will become charter members.

R. MacD.

AMA STUDIES UNIFORM CHEMICAL LABELING LAW

A program to protect the public from the dangers of mislabeled household and commercial chemicals recently was launched by the American Medical Association. Through its Committee on Toxicology, the AMA is gathering information on existing state labeling regulations with the idea of developing model legislation on the precautionary labeling of various chemical products — such as paints and paint removers, heating and cooking fuels, household polishers and cleansers, laundering items, etc. — which are not now so regulated. The end result would serve as a guide for writing uniform regulations requiring labels to show information on the product's contents, its possible dangers, directions for safe use, and first aid instructions.

Bernard E. Conley, Ph. D., Committee secretary, reports that there are at least a quarter of a million different trade-name substances now on the market. Without proper labeling, both physicians and the public may be uninformed about harmful materials these products contain and the ways of treating poisonings from them.

Other organizations, including the American Academy of Pediatrics, American Public Health Association, American Pharmaceutical Association, National Safety Council, leading trade associations and various state and national governmental regulatory agencies are being consulted on this problem and its solution.

FOUNDATION FOR EYE CARE

Announcement was made on November 15 of the establishment of the National Medical Foundation for Eye Care, a non-profit scien-

tific and educational institution, incorporated in New Jersey. The Foundation has been organized by ophthalmologists of the country to provide American ophthalmology with an agency to present to the public generally and to fellow physicians pertinent information on the care and treatment of the eyes.

Dr. Ralph O. Rychener of Memphis is president of the Foundation; Dr. Edwin Forbes Tait of Norristown, Pa., vice-president, and Dr. Charles E. Jaeckle of East Orange, N. J., secretary-treasurer.

The object and purpose of the Foundation is to advance the public welfare by:

1. Gathering, receiving, assembling and studying information relative to eye care.
2. Fostering or engaging in investigations and research in all aspects of eye care.
3. Sponsoring studies of educational, socio-economic and scientific factors affecting eye care.
4. Issuing reports and otherwise disseminating information relative to eye care to the general public and to members of the medical profession and ancillary workers.
5. Promoting the conservation of vision and the prevention of blindness through the wider dissemination of knowledge of the eye, its defects, dysfunctions and other diseases and their relation to general health.
6. Promoting a more effective utilization of the scientific knowledge of ophthalmology and the other related branches of medicine.
7. Generally performing any act, related to the foregoing, designed to present to the public generally and the medical profession, all pertinent information on the care and treatment of the eyes.

YOUR JOURNAL

Recently the editorial board of the Delaware State Medical published an editorial setting forth the policy of that journal. As the statements seem applicable to our own journal, they are borrowed here for the information of our readers.

"The primary function of a State Journal is to publish medical news, the proceedings of the House of Delegates and the scientific papers read at the Annual Meeting.

A State Journal should be a general journal, published for the benefit of physicians of varied interests. For this reason, articles limited to reports of detailed research that would interest only a small number of individuals have no place in this type of journal. Instead, the review article is a more suitable medium to keep the average physician informed of the progress occuring in other branches of medicine.

It is our belief that the review article is of great value and interest and we have arranged for articles on various subjects to be written by medical teachers. These will appear monthly under the heading of "Medical Review". The first three review articles will be written by local physicians because of their willingness to submit material in time to meet the publication schedule; this fact is offered as an explanation, not an apology.

A State Journal should provide an outlet for publication of material written by local physicians. It is doubtful, however, if any journal could long survive on such a limited diet. There is a need for articles written by physicians from other localities, particularly from teaching centers. Maintaining a proper balance between these different types of material is a primary duty of the editor and his associates.

Finally, we believe in the case report. This valuable medium of expression should form the backbone of any local journal. It is unfortunate that most physicians are deterred from contributing to the literature through this medium by the mistaken idea that the case report is a thing of the past. They think that a case report should include a detailed review of the literature but this is not true. A short, concise case report without review of the literature is a highly desirable item.

This is your Journal. Tell us what you want."

Delaware State Med. Jour., July 1956.

Dr. C. H. Peebles, Jr., Lee County native has recently become associated with Dr. Joseph B. Workman at 1673 Brabham Avenue, Columbia, in the practice of Ophthalmology.

He was graduated from the Medical College of South Carolina in the class of 1951. He interned at St. Francis Hospital, Pittsburgh, and completed a residency in Ophthalmology at McPherson Hospital, Durham, North Carolina.

BLUE CROSS . . . BLUE SHIELD

Something about the Blue Shield Fee Schedule

We in South Carolina Blue Shield have been in the habit of referring to our surgical schedule of allowances as a $150.00 fee schedule. This statement was based upon a faulty conception of the factors which determine a designation of the schedule classification. We have been basing our designation solely upon the fact that our schedule contains allowances up to $150.00 and none higher than that figure. Because of the fact that we ourselves label our schedule as a $150.00 schedule, we have invited unfavorable comparisons between our schedule and those of other Blue Shield plans and of commercial contracts. Using the method we have used to label our schedule, if we had assigned an allowance of $200.00 or $300.00 to even a very few procedures, we could have labeled our schedule a $200.00 or a $300.00 schedule.

Actually our schedule and those of many other Blue Shield and commercial insurance companies have been tagged with a maximum fee allowance, and other allowances bear no constant or uniform relationship to that maximum fee, except that they do not exceed it. The allowances set by us for less major procedures are rationally in line with a $200.00 schedule, and many of them are in line with an even higher schedule.

Every surgeon, either deliberately or unconsciously, grades his charges according to the difficulty, the operating time, the skill required, and perhaps other factors involved in handling his cases. He has developed in his thinking a schedule of relative values, and his schedule of charges is more or less balanced.

Blue Shield has no such system or schedule of relative values, and therefore its fee schedule is badly out of balance. The unbalance applies most strongly to the more difficult procedures, so that the surgeon whose practice includes a high proportion of highly technical procedures is penalized by a fee allowance of $150.00 — just $50.00 more than the allowance for a relatively simple appendectomy or a salpingectomy.

There has been a growing realization that insurance carriers need some kind of relative value schedule similar to that used either consciously or unconsciously by every surgeon. In 1952 the California Medical Association undertook to do something about this need. The Association set up a committee "to develop a set of guiding principles which should govern the development of fee schedules." It took the committee three years to complete its assignment.

The standards for relative values of fees were established by the committee by survey of the membership. It found that the level of fees varied throughout the State. The analysis of the survey results reveals that the relationship between fees for most procedures remains almost the same.

Forty-seven hundred California physicians responded to the survey. Their replies were subjected to a number of statistical analyses. Suggested fees for each of more than 2500 procedures or services, including medical, surgical, anesthetic, radiological, pathological, and chemical were studied. The *average* of the suggested fees for any one procedure was not used. Instead, the *median* and *modal* figures were ascertained. From these figures, a schedule of relative values of medical services, another for surgical services, another for radiological services, and a final one for pathological examinations were compiled. The Relative Value Schedule of the California Medical Association was thus arrived at.

Two other studies of a means to arrive at a relative value schedule have been reported. The first was by Dr. William H. Horton, Executive Director and Director of Medical Services, Connecticut Medical Service (Blue Shield), and the other was by the Economics Committee of the Montana Medical Association. Each study used a formula devised by Dr. Horton. The results of the two studies are closely parallel. Interestingly enough, the service indices, as labeled by Dr. Horton, bear a relationship to each other very nearly approximating that of the relative value indices of the California schedule.

Neither of these schedules is a fee schedule. They state no fees. They set up a scale of values applicable to a series of procedures, so that if a fee in dollars is set for any one of them, relative fees in dollars may be determined for any other of the group.

By applying such a schedule of relative values, a balanced schedule can be determined. Thus, Blue Shield plans are provided a tool of tremendous value in setting up fee schedules, provided only that participating physicians will accept the relative value schedule as a basis for fixing fee allowances.

The South Carolina Medical Care Plan is attempting to balance and modernize its surgical fee schedule. To do so will necessitate either one of two things: Either fix a maximum fee allowance for the most technically difficult procedures, and then work back, using the relative value formula, to the most minor procedure covered by the schedule; or make a fee allowance for some lesser or intermediate procedure and apply the relative value formula to procedures above and below the selected basic procedure. Should a maximum fee of $200.00 be assigned, then each unit value in the relative value schedule will be 2, and some representative dollar fees would be: appendectomy, $70.00; oophrectomy, $80.00; abdominal panhysterectomy, $120.00; transurethral

electro-resection of prostate, $140.00; nephrectomy, $140.00; hemorrhoidectomy, $50.00; subtotal gastrectomy, $140.00; tonsillectomy, $30.00; cholecystectomy, $110.00; inguinal herniorrhaphy, $90.00; incision and drainage of boils, furuncles, and surface abscesses, $2.00; small skin grafts, $10.00; large grafts, $60.00; fracture of femur, simple reduction, $90.00; Colles' fracture, $45.00.

A comparison of these fees with our present schedule will indicate how unbalanced our schedule is.

If we should apply a unit value of $5.00, in order to set a minimum allowance of $5.00 for minor surgical procedures we would come up with about 100 procedures which would rate a fee of $500.00. Such a $500.00 schedule would necessitate at least a doubling of present Blue Shield membership dues. It may be that we shall have to resort to the method set up by the Medicare contract and use a variable unit value, a greater one for minor procedures and a lesser one for major procedures. Many of us believe that it is important not to materially increase dues for Blue Shield membership under our present relatively low income service benefit contract, although we would not be adverse to an alternative contract with higher income limits for service benefits and with a materially higher fee schedule and at a real increase in cost to the subscriber.

J. Decherd Guess, M. D.
Medical Director

THE SOUTH CAROLINA ACADEMY OF GENERAL PRACTICE

TO ALL DOCTORS IN SOUTH CAROLINA

The South Carolina Academy of General Practice and the South Carolina Medical Association lost one of its distinguished members two years ago when Dr. W. L. Pressly died. Since that time the South Carolina Academy of General Practice has been thinking of a plan to do honor to the memory of Dr. Pressly.

It has been called to our attention that each year four or five students at the Medical College of South Carolina run into financial difficulties for various reasons beyond their control. These students find it very hard to remain in school without help.

It is our desire to help these students by establishing a loan fund in Dr. Pressly's memory. It is planned that these students can borrow from this fund up to five hundred dollars a year, without interest, for the remainder of their medical course. Three years after internship they begin making yearly payments until the loan is repaid.

To raise the initial capital, $5000.00, the South Carolina Academy wishes to invite all doctors in South Carolina to make a contribution to the fund.

Dr. Pressly, known to his many friends throughout the state as "Buck," did a great service to the state of South Carolina during World War II by serving as chairman of the procurement and assignment service for South Carolina. He received many honors during his medical career. He was President of the South Carolina Medical Association in 1941. He brought distinction to South Carolina Medicine by being chosen "Doctor of the Year" by the American Medical Association in 1948. We are proud that he was a charter member of our South Carolina Academy of General Practice.

The South Carolina Academy of General Practice is now eight years old, has a membership of 280 and is growing steadily. After the initial capital for the fund is raised we plan to keep it going by yearly payments from the academy. We wish to honor your friend and our friend and member by establishing a loan fund at our Medical College to be known as "The W. L. Pressly Memorial Loan Fund." This fund will be of great service to young men who need help financially. We can think of no better way to honor Dr. Pressly and we invite your contributions. Please make checks payable to "The W. L. Pressly Memorial Loan Fund" and mail to Dr. Horace M. Whitworth, 301 E. Coffee St., Greenville, S. C.

Kirby D. Shealy, M. D.
Committee Chairman

REPORT OF A DELEGATE TO THE HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION IN CHICAGO, 1956

(Continued)

A good number of physicians from South Carolina were present at the meeting. It is always an eye opener to one who has never attended a meeting of the House of Delegates and more especially a reference committee. Every physician is welcome and is urged to take part in the discussion in the reference committee meeting.

THE CONFERENCE OF PRESIDENTS AND OTHER OFFICERS OF STATE MEDICAL ASSOCIATIONS

(Sunday before the regular meeting of the House of Delegates)

Guthrie Y. Graves of Bowling Green, Kentucky, newly elected president of this organization, gave the first talk on the Medical Practitioner—Yesterday, Today, and Tomorrow. Hé brought out the difference between practice with horse and buggy and bad roads fifty years ago and automobiles and good roads today. He pled for less of the stuffed shirt attitude among physicians especially as to their patients. He pointed out that today less than .6% of the population live more than 25 miles from a doctor. He urged that the

small hospitals take more responsibility in training nurses even if for only the first year or two. He suggested what has already been done in a great many places that small hospitals hire pathologists and radiologists together. No one could pay enough for the entire service of either but with several together it could easily be managed. As a surgeon in a relatively small community he made an excellent plea for and pointed out methods by which better medical practice can be developed.

The second speech was unique and one of the most inspiring that I have ever heard. I'm sure everyone else was similarly affected because at the end everyone in the audience stood and applauded loud and long. There is no way to put in print the earnestness and sincerity with which the speaker talked. He was Henry Viscardi, Jr., President of Abilities, Inc. That is the firm which hires only what we refer to as disabled people. He says, and he should know, that there are no disabled people—just men and women and boys and girls. By this he means that the man or woman who is emotionally unfit to get along with people is just as disabled as a man whose joints are permanently stabilized with arthritis.

His Company was started in 1952 with four people "disabled" like himself. It is a company which makes precision parts for electronic instruments. They agreed that only disabled people would be hired, that they would sell in a highly competitive market, that they would seek no sympathy or security, but opportunity to work and produce. After a year the company netted $52,000.00 and paid off an $8,000.00 loan and had 59 employees. The second year 129 employees and grossed over $400,000.00; the third year 168 empolyees and $600,000.00. Today, in the fourth year, 276 people and they expect to gross $1,200,000.00. Some slides were shown of different employees. One girl who at 32 went out of the house for the first time since she contracted polio at 7 years of age. Another blind man who laces cables, a highly complicated procedure. A skilled artisan with fixed joints who cannot sit down because of his fixation but must stand, lean, or sit against something. The only complaint he ever made was when they asked him to work only eight hours instead of overtime to ten as the plant usually has to operate. The average pay is $1.69 per hour and rising. They lose an average of three employees a month to what they affectionately term their competition—General Electric, Westinghouse, and Sperry Gyroscope.

Mr. Viscardi was born without knees or feet and spent the first seven years of his life in a hospital. He has a deep and enduring and professed love of the medical profession and intends to spend the remainder of his days working with the medical profession in an effort to assist in rehabilitation. He never walked alone until he was 27 years old. As a child he asked his mother why, why did this happen to him. His mother replied that God had a meeting with his councilors and decided that the Viscardis would be a fine family to give a disabled child to.

It was he who rocked the august Senate finance committee when he told them that there were no disabled persons, that the dole has a deadening effect. The committee apparently was as moved as his audience was that Sunday afternoon because he was urged to tell more. What a pity that everyone, especially the disabled or pseudo-disabled, could not hear him. The effect that he produces cannot be believed until one has heard him. He wound up his talk by saying that "neither pensions, parades, or pity, but the sweet dignity of productivity" is what the disabled person wants.

The next speaker was Governor Howard Pyle (formerly Governor of Arizona) and now Administrative assistant to the President. He urged that the medical association take the lead and be prepared with information on all possible subjects that are apt to come up. It is not enough, indeed it is a poor policy, to always be against something. Much better to be for something constructive. He pointed out that the pressures on a member of Congress are unbelievable, that it is difficult to keep one's sense of balance and judgement because of these arguments pro and con. He repeated several times that the medical profession cannot afford to sit back, but must be a positive force for the betterment of the health of the citizens of the United States. Governor Pyle pointed out that from bondage one develops spiritual growth. From that courage, then freedom. From freedom we are apt to relax our vigilance and initiative and go to dependency. From dependency it is only a short step to bondage again — and so the cycle repeats itself — as history does. Where are we in this cycle, and what are we doing about it?

The last speaker, Dr. Alan Stockdale, spoke on "The Healer Goes Forth." He was a minister till he was 62 years, has been the Dean of speakers for the National Association of Manufacturers. His theme was better public relations for physicians. He stated that if the public knew the truth about doctors they would love them. He suggested hiring the best publicity men in the business, the best journalist to tell the story of physicians.

As some of the wrong thinking he pointed out juvenile delinquents are said to number about 435,000 but who, he asks, writes and talks about the 15,000,000 good kids. We talk about the 4,000,000 unemployed but we should talk about the 65½ millions who are working. He said we as physicians need the kind of salesman who was in the dairy supply business. He sold a farmer with one cow two milking machines. That, he said, is salesmanship. Then he took the cow as a down payment on the two machines. That's supersalesmanship. Dr. Stockdale paid tribute to the ideas expressed by the previous speakers and terminated the program by assuring the doctors that we must present a better front to the public.

INAUGURATION CEREMONY

In the Chicago Civic Opera House Dr. Dwight Murray of Napa, California, was inaugurated as President of the American Medical Association.

In his speech he urged doctors to be more deliberate with their patients, to take time to talk with and listen to them. He urged patients to pick out a good doctor, have faith in him, and stick with 'im. It was televised over the local station as was the ceremony in Atlantic City last year.

Dr. Walter Bierring, eighty eight years old, was given the 1956 Distinguished Service Award for his long and faithful efforts in behalf of medicine in general.

SPECIAL ARTICLES

CLEFT PALATE CENTER

Dear Doctor Waring:

Enclosed please find an outline of both the operation of the Cleft Lip and Cleft Palate Center and of our five year study of the unoperated cleft palate case. This was written more from the layman's point of view than from the physician's.

The findings of these unoperated clefts of the palate and their referral to us by the practicing physicians of the State is now the only limiting factor in carrying out this study. I would like to invite all the physicians of the State of South Carolina to consider themselves as active participants in this research project, the successful prosecution of which will add to our general knowledge, to our ability to better care for these patients, and to the prestige of both the Medical College and the professional membership of the State.

Sincerely,

Robert F. Hagerty, M. D.

A center for the care of cleft lip and cleft palate patients has been initiated at the Medical College of South Carolina in Charleston. Approximately one in every 700 births is a cleft lip, cleft palate, or combination of the two, and so this entity represents an important one in the population at large. Fortunately, much can be done to help those afflicted with this deformity, both in regard to their appearance and function.

The cause of this congenital anomaly is unknown, but apparently occurs during the first months of intra-uterine life. The cleft lip is usually repaired at age three months with a resulting marked improvement in appearance and also in that area of speech determined by the lips. The cleft palate is repaired surgically at about two years of age just before the child commences to talk. To defer operation beyond this time is inadvisable because bad speech habits are formed with the unrepaired cleft, which are difficult if not impossible to eradicate later. With surgical repair of the palate, the nasal cavity is again separated from the mouth, making speech much more normal and preventing the loss of fluid and food through the nostrils.

In the treatment of such a deformity as cleft palate which involves a complicated anatomical area, the knowledge of many specialties in addition to that of plastic surgery is necessary. The speech therapist plays a most prominent role because the cleft palate is primarily repaired to improve speech and it is the resulting speech which is all important to the patient, and determines the success of the operation. Tape recordings of speech are taken preoperatively and at intervals postoperatively to determine the patient's progress. The speech therapist is most effective in helping the patient learn to use his newly repaired palate and plays a most important role in this rehabilitation program. We are most fortunate in having a speech therapist, Mr. Milton J. Hill, who is vitally interested in this aspect of speech therapy and who has had considerable experience in this field in one of the national centers in Pennsylvania. An ENT specialist also plays a prominent role in diagnosing and treating the malformation and disturbances in the ears, nose and throat secondary to the cleft deformity. A dentist and prosthodontist, together with the orthodontist participate in this team, taking dental study models and fitting the patients with a dental prosthesis when necessary. A general examination is given by a general physician or pediatrician. Roentgenograms of the skull are taken with special equipment in which the head is fixed in true A. P. and lateral positions. In this way measurements and angles can be derived and compared with normals to determine abnormalities in facial growth. A careful mental examination is also carried out so that the patient's progress can be correlated with his abilities.

Care of the cleft palate patient therefore is carried out by a team, including a plastic surgeon, speech therapist, ENT specialist, dentist, prosthodontist, orthodontist, pediatrician, roentgenologist, and psychologist. Each member makes his evaluation of the patient and the therapy to be carried out is decided at a round table discussion.

Recently there has been an attack on the time honored procedure of surgically repairing the cleft palate during the second year of life. It is claimed by a small but vociferous group that such early surgery will damage growth centers of the facial bones, producing a lack of growth of the mid-face resulting in a dish-faced deformity. The arguments to defer surgery until later years are not based on sound scientific fact. As a matter of fact, seriously crippling habits of speech can be formed by such a delay. In order to throw some light on this important subject we have been given a generous grant from the National Institutes of Health to study the cleft palate patient be-

fore operation. It is only by a study of the unoperated cleft palate patient, especially in regard to his facial growth, that we can tell what part surgery plays in this regard. Abnormalities in facial growth are very probably related to the congenital anomaly itself. It is therefore reasonable that we must have a sound knowledge of the abnormalities in the unoperated case before attributing these abnormalities to surgery.

With the cooperation of Dr. G. S. T. Peeples and Dr. R. W. Ball of the State Health Department, we are carrying out a thorough examination of the unoperated cleft palate patient over the age of seven years. As a result of our grant we are able to carry this out without charge to the patient. The examination requires the greater part of a Saturday morning. After all the necessary data have been compiled and reviewed, each individual case is discussed by the team and recommendations are forwarded to him and to his family physician. There are agencies in the State to help with the cost of his hospitalization and surgery should it be necessary. Funds are available for transportation to Charleston and even for boarding overnight, if that is necessary.

It is thus seen that our work at the Cleft Lip and Cleft Palate Center of the Medical College of South Carolina is not only scientific investigation, but also embraces a program of care to the patient. It is hoped that all those with an unoperated cleft palate over the age of seven will take advantage of this opportunity by contacting their family physician for an appointment for examination at the Cleft Lip and Cleft Palate Center, Medical College of South Carolina, Charleston, South Carolina.

Robert F. Hagerty, M. D.
Director, Cleft Lip and Cleft Palate Center
Assistant Professor of Surgery (Plastic Surgery)

TUBERCULOSIS IN SOUTH CAROLINA TODAY

FRANK L. GEIGER, M. D.
Columbia, S. C.

1. 300,000 South Carolinians infected with tubercle bacilli (estimated)
2. 2,297 known active cases
3. 3,195 known inactive cases
4. 1,024 known active cases not hospitalized
5. 592 known active cases at home with positive sputum or sputum status unknown
6. 228 deaths from tuberculosis in 1955
7. 925 new active cases reported in 1955

The above shows that the tuberculosis problem is still with us and that we still need to be concerned. A pertinent factor which must not be lost sight of is the communicability of tuberculosis.

It is true that there has been an accelerated decrease in the mortality rate during the past ten years. Further, the change in age distribution of tuberculosis deaths has been significant during this same period. The number of tuberculosis deaths among persons 25 years of age or younger decreased markedly. Most of the deaths now occur among persons 40 years of age or older. As expressed by Dr. James J. Waring, "Tuberculosis has been converted from a 'killer' to a 'crippler'." Tuberculosis is less and less a mortality problem and more and more a morbidity problem. The dead "lunger" no longer spits tubercle bacilli but the "lunger" inadequately treated by miracle drugs with or without surgery, remains alive and potentially a spreader of disease.

Every physician, whether in general practice or a specialty, can and should actively engage in the tuberculosis control program. In the history of man, the present offers the greatest hope for the ultimate eradication of this disease. The physician will carry not only the primary responsibility of diagnosis, as he always has, but will be concerned to a larger extent than ever before with treatment and follow-up.

Diagnosis: In this state facilities are available for the diagnosis and subsequent follow-up of all patients. Roentgenographic equipment is available in the private offices of roentgenologists, in hospitals, in sanatoria, in local health departments and in the offices of many private physicians. Old tuberculin, and mailing containers with sputum bottles, are available to private physicians, from the State Health Department, upon request. All sputum specimens submitted to the State Board of Health's Laboratory in Columbia are examined by smear and culture for tubercle bacilli.

Treatment: After the diagnosis of active tuberculosis is made by the physician, wherever possible and when beds are available it is advisable that treatment be initiated in a tuberculosis sanatorium. Preferably the treatment of the active tuberculosis case should be continued in the tuberculosis sanatorium until the disease is satisfactorily stabilized. In the tuberculosis sanatorium the patient will also have the benefit of recreational and occupational therapy, educational, medical, social and rehabilitation services.

Those patients whose disease responds to sanatorium treatment and their tuberculosis becomes inactive, although antimicrobial therapy must be continued, can be safely discharged to their homes, provided their physicians will accept the responsibility of their continued treatment and follow-up.

As far as the antimicrobial drugs are concerned there is general agreement that:

1. Two drug combinations are almost always used.
   (a) Isoniazid (4-5 mg. per kg. of body weight, usually 150-300 mg. daily given in 3 divided doses, after meals), and sodium PAS

(12 grams daily).

or

(b) Isoniazid and streptomycin (1 gram, 2-3 times a week).

or

(c) Streptomycin and sodium PAS.

Recalcitrant Active Tuberculosis Patients:

There is a legal basis in South Carolina for compulsory isolation in the tuberculosis sanatoria of recalcitrant individuals with active tuberculosis. This law has been used frequently to commit these individuals, but because facilities for confining them are not adequate many leave the sanatoria against medical advice and with positive sputa. It appears, to this writer, that it is imperative that locked wards be provided at the State Tuberculosis Sanatoria, or that a separate facility be erected for confining these uncooperative, stubbornly rebellious persons with active tuberculosis, if the goal of eradication of tuberculosis in this State is to be achieved.

NEWS

Dr. Edwin B. Parkinson has opened an office at 14 Medical Court, Pendleton Street, for a practice limited to obstetrics and gynecology, the Greenville County Medical Society has announced.

A native of Due West and graduate of Erskine College, he attended the University of North Carolina School of Medicine and was graduated from Jefferson Medical College of Philadelphia in 1945. He interned at Pennsylvania Hospital and then served a four-year residency in obstetrics and gynecology at that hospital and at Lankenau Hospital.

He served in the U. S. Air Force medical corps for two years as a captain.

Since February, 1953, he has been an associate in gynecology at the Medical College of Virginia and on the staffs at the college's hospital and Stuart Circle Hospital, Richmond, Va.

The establishment of an approved school of medical technology for training of technicians by the central laboratory of the State Board of Health was recommended in a resolution adopted by the executive committee of the State Board of Health at a recent meeting.

Dr. G. S. T. Peeples, state health officer, said the resolution approved the idea of establishing a school to train medical technicians in the board of health laboratory.

Such a school would be conducted in affiliation with the clinic at the Columbia Hospital and the bacteriological department at the University of South Carolina. The proposed training would lead to a degree in the medical technician field.

Dr. John A. Boone of Charleston has been elected to a three-year term on the National Board of Directors of the American Heart Association.

Dr. David D. Moise of Sumter has been elected chairman of the South Carolina Regional Blood Committee, which administers the Red Cross blood program in 20 central South Carolina counties.

A. M. Robinson, M. D. announces the removal of his office to 1513 Hampton Street, Suite 1-B, Columbia, South Carolina.

The Ninth Annual American Academy of General Practice Scientific Assembly, will be held on March 25-28, 1957, in Kiel Auditorium, St. Louis.

Dr. Alton Brown of Rock Hill was elected president of the South Carolina chapter, American College of Surgeons, during the annual meeting at the Medical College of South Carolina on November 16.

In addition to Dr. Brown, who succeeds Dr. Edward F. Parker of Charleston, other officers named to one-year terms were Dr. James B. Martin of Charleston, vice president; Dr. Furman Wallace of Spartanburg, re-elected secretary-treasurer. Named to the council were Dr. Frederick E. Kredel and Dr. Parker of Charleston, Dr. C. J. Scurry of Greenwood, Dr. A. T. Moore of Columbia and Dr. L. H. McCalla of Greenville.

Dr. Paul Colonna, Professor of Orthopedics from the University of Pennsylvania spoke at the last meeting of the South Carolina Orthopedic Association as well as the meeting of the Richland County Medical Society, at which time he talked on CONGENITAL DISLOCATIONS OF THE HIP. Dr. Colonna was introduced by Dr. William A. Boyd, who gave a brief talk on progress in Orthopedic Surgery in the last half century.

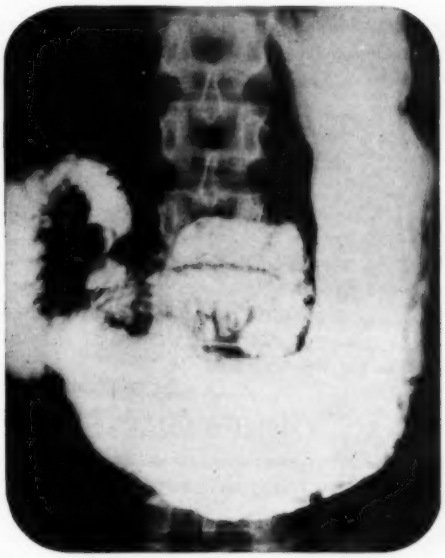
For the second time a Consecutive Case Conference (Pembine type) was sponsored by the Trudeau Societies of South Carolina, Georgia, and Florida, and held at Ponte Vedra Beach, Florida, on October 26, 27 and 28. Cases were presented from the South Carolina Tuberculosis Sanatorium, State Park, by Dr. Charles E. Gill and from Pinehaven by Dr. David B. Gregg. Dr. Eugene Y. Smith, Jr. of Charleston was elected Chairman of the Steering Committee for the third Tri-State Conference to be held at Ponte Vedra, October 18 and 19, 1957.

At the Annual Meeting of the South Carolina Trudeau Society held on October 17, the following new officers were elected: President, E. Alex Heise, M. D., Sumter, S. C.; Vice-President, Frank L. Geiger, M. D., Columbia, S. C.; and Secretary-Treasurer, John M. Preston, M. D., Columbia.

DIAGNOSTIC AID

Reduced Hypermotility with Pro-Banthine® Improves Visualization

*Posterior-anterior film: definite hyperperistalsis with poor duodenal visualization.**



Posterior-anterior film after 15 mg. of Pro-Banthine intramuscularly: chronic duodenal ulceration clearly disclosed.

The same anticholinergic action which has made Pro-Banthine (brand of propantheline bromide) the outstanding therapeutic agent in peptic ulcer has also proved valuable in diagnosis.

By controlling the hypermotility, Pro-Banthine may permit delineation of a lesion otherwise not clearly visualized.

The technic is simple: If the first set of films shows hypermotility but no filling defect is demonstrable, reexamination is done a few minutes after intramuscular injection of 15 mg. or a half hour after oral administration of 30 mg. of Pro-Banthine.

This procedure has the additional advantage of demonstrating the patient's response to a given dosage of the drug.

G. D. Searle & Co., Chicago 80, Illinois, Research in the Service of Medicine.

*Roentgenograms courtesy of I. Richard Schwartz, M.D., Kings County Gastrointestinal Clinic, Brooklyn, N. Y.

SEARLE

Dr. Charles E. Aimar of Charleston is to be associated in the general practice of medicine with Drs. J. McI. Willcox and M. J. Coleman in Darlington.

A native of Charleston, he was graduated from the Medical College of South Carolina in 1953. He served his junior internship at Roper Hospital in Charleston and interned at Philadelphia General Hospital from 1953 to 1954; and was house resident physician at Mullins hospital for three months in 1954 before entering the Navy as a lieutenant in the medical branch.

A new law banning the practice of naturopathy in South Carolina apparently will become effective soon.

The U. S. Supreme Court has refused to hear an appeal from a group of South Carolina Naturopaths against the law enacted by the 1956 General Assembly.

South Carolina courts previously upheld the law.

The U. S. court said it found no substantial federal question involved.

The State Supreme Court said the legislative act was "a valid exercise of the police power of the state."

Requirements for the treatment of illness and disease, the state court said, "is not a judicial question. It is one of legislative authority"

ANNOUNCEMENTS

The Academy of Medicine of Cincinnati cordially invites all physicians, their families, and their patients to its 100th Birthday Party, February 27 through March 5, 1957. In order to officially observe the occasion, a Health Museum and Exposition will be established in Cincinnati's spacious and historic Music Hall. One hundred and seventy-five health and scientific exhibits, representing medicine, hospitals, research centers, public health, nursing, pharmacy and industry will be displayed. Notable among these exhibits will be an atomic energy exhibit from the American Museum of Atomic Energy entitled "Atoms for Peace."

"Juno", a full-sized, activated manikin, graciously loaned for the occasion by the Dominican Republic, will be on display. Juno is operated electrically, and with concurrent recorded narration, will demonstrate blood vessels, bones and organ structures of the body.

Dr. Paul D. White and Dr. Walter Alvarez, noted medical scientists and authors, have accepted invitations to be among the distinguished guest speakers.

The Centennial Convocation will be held on the last night of the Exposition, March 5, 1957. The Convocation address will be given by Sir Edward Appleton, Nobel Laureate, Edinburgh, Scotland, and civic leaders, officials of both the American and State Medical Associations, and Government dignitaries will take part in the elaborate ceremonies.

DEATHS

DR. HAL T. THOMAS

Dr. Hal T. Thomas, 56, resident staff physician at State Park Sanatorium, died suddenly of a heart attack on October 19. Dr. Thomas had been a staff member at the South Carolina Sanatorium for a number of years.

DR. FRANK R. WRENN

Dr. Frank R. Wrenn, 72, widely known radiologist and for many years president of the Anderson Memorial Hospital, died October 11, 1956.

Dr. Wrenn came to Anderson in 1919 as the first radiologist at the Anderson Memorial Hospital. He was a pioneer in this field and in the development of that hospital during his many years of service.

During his residence in Anderson Dr. Wrenn was active in religious, civic, and fraternal affairs of the community.

A native of Siler City, N. C., he was born August 31, 1884.

DR. JAMES EDGAR DOUGLAS, JR.

Dr. James Edgar Douglas, Jr., of Winnsboro, died November 17.

Dr. Douglas was born in New Hope community of Fairfield County July 28, 1892. He was graduated from Erskine College and the Medical College of South Carolina.

He practiced medicine at Winnsboro from 1920 until the time of his death.

BOOK REVIEWS

THE PERSON BEHIND THE DISEASE, by Julius Bauer, M. D. pp 136. Grune and Stratton, New York 1956.

This recent summation is an able presentation of the author's well-known and provocative ideas on the constitutional, hereditary and psycho-somatic influences in various disease states. While the verbiage is at times somewhat involved, the serious student who is interested in the broad philosophic concepts of what makes a man what he is will find much to cogitate upon. This book is not aimed at those interested in practical therapeutics but rather at those who are trying to understand "what makes Tommy run?". The book contains an adequate bibliography for pertinent current literature and a modest index. It is recommended for the reader oriented to the gene, the id, the ego, and the total personality as related to the problem of the sick person. No psychiatrist nor psychosomatacist should be without it. Many of us ordinary doctors will read it with profit.

Fred Kredel, M. D.

COLLAGEN DISEASES, John H. Talbott, M. D., and R. Moleres Ferrandis, M. D. New York-London, Grune & Stratton, 1956, 232 pages. $6.50.

This monograph deals with a limited group of diffuse collagen diseases with a grave prognosis. They have reached increased prominence because of their unknown etiology, their relative newness to many physicians, new therapeutic agents that may alter their course and an apparently increased incidence in the last 10 years. The diseases included in this monograph are systemic lupus erythematosus, polyarteritis, dermatomyositis, systemic scleroderma and thrombotic thrombocytopenic purpura.

The authors incite the reader with enthusiasm for more knowledge of these closely related and interrelated disease entities by giving in the preface, a finger nail sketch of their appearance in medical literature by different well known medical figures at different times, and their enthusiastic response to one and another's observations. They continue in their introduction to be more specific in their description of this group of diseases and their relationship to one another. It is at this time that it can be sensed that a clear differentiation and understanding may not be reached.

The authors have made an attempt to produce a concise monograph on these five collagen diseases. Their writings are based to a certain extent on personal observations, discussions and reflections over the past 20 years, but to a major extent on an extensive review of the literature. To substantiate this statement is a recorded bibliography of 540 references which are referred to virtually at the end of almost every sentence.

The monograph does leave the reader better informed, the degree depending on his pool of knowledge before reading. He is stimulated to learn more about these intriguing diseases that defy his diagnosis, understanding and treatment. He is left with a valuable source of reference material to delve into with specific references to individual points, and a very good summary of the individual entities.

Thomas A. Anderson, M. D.

PROCEEDINGS, WORLD CONGRESS OF ANESTHESIOLOGISTS, edited and published by the International Anesthesia Research Society, Burgess Publishing Company, Minneapolis, 1956. Price $5.00.

The world's largest international Congress of Anesthesiologists was held at Scheveningen, The Netherlands, September 5-10, 1955. Most of the scientific papers read at the meeting have been published as the Proceedings by the International Anesthesia Research Society. The papers were presented in English, French, or German, and many of the original articles subsequently were published in medical journals in their native language, yet, all of the papers appearing in the Proceedings have been translated into the English language. Each author and title will be indexed in the Quarterly Cumulative Index Medicus and the Current List of Medical Literature, Armed Forces Medical Library.

The speakers who appeared on the program came from many countries throughout the world. Each was chosen because of his outstanding clinical work with some particular anesthesia drug or technique, or because of his research contributions within a field directly related to anesthesiology. The excellent assortment of scientific papers reflects extensive efforts of the Program Committee to present both the research and the clinical aspects of anesthesiology to the assembly.

Among other contents, this volume contains heretofore unpublished laboratory data on recent anesthestic drugs and techniques, a survey of the academic and clinical status of anesthesiology in many of the foreign countries of the world, and detailed instructions for the clinical use of many infrequently employed techniques such as hypothermia, artificial hibernation, and hypotensive anesthesia. Consequently, the Proceedings appears to be of greatest interest to the anesthesiologist who has already acquired a background knowledge of the fundamentals of anesthesiology.

John M. Brown, M. D.

PROGRESS IN PSYCHOTHERAPY 1956. Edited by Frieda Fromm-Reichmann and J. L. Moreno, 340 pages. Grune & Stratton, New York. Price $8.50.

This book is probably the first attempt to gather together all the various divergent theories and practices of psychotherapy. In effect, it puts down in precise, reasonably brief form, the main thoughts and practices of all the leading psychoanalytic schools. The goal of this book is four-fold.

First, it attempts to establish in stronger, clearer tones, the rising importance of the psychological approach to the overall problem of psychiatric therapy. To this extent it has the advantage of making psychoanalysis not a separate part of psychiatry, but a very integral part of all psychiatric practice.

Second, it studies not the differences, but the similarities between the various schools of psychotherapy or psychoanalysis. Third, by stressing the importance of the doctor-patient relationship, it makes the psychotherapeutic experience a special personal experience in which all parts of the patient's emotional life, no matter how trivial or seemingly unimportant, are seen as distinctly related to all aspects of emotional life.

Fourth, this book breaks through the sense of former hopelessness about the treatment of psychotic patients and shows conclusively that psychotherapy is a vital and growing force as it reaches out to more and varied types of psychiatric problems.

This book could be of interest to all doctors since it discusses and demonstrates psychotherapy on all levels of practice with a special emphasis on the mechanisms of therapy, rather than an intellectual discussion on theory. Norton L. Williams, M. D.

Digitalis

in its completeness

Each pill is equivalent to one USP Digitalis Unit

Physiologically Standardized therefore always dependable.

Clinical samples sent to physicians upon request.

Davies, Rose & Co., Ltd.
Boston, 18, Mass.

ADVERTISERS

Abbott Laboratories
Allen's Invalid Home
American Bakers
American Meat
Ames Company
Appalachian Hall
Ayerst Laboratories
Bayer Company
Brawner's Sanitarium
Broadoaks Sanatorium
Burroughs-Wellcome & Co.
Cambridge Pharmaceuticals
Columbus Pharmacal Co.
Davies, Rose & Co., Ltd.
Eli Lilly & Company
Estes Surgical Supply Co.
Foot-So-Port Shoe Co.
Geigy Pharmaceuticals, Inc.
Highland Hospital
Knox Gelatine Company
Lakeside Laboratories
Lederle Laboratories
Merch, Sharp & Dohme
Parke, Davis & Company
Pfizer Laboratories
Physicians Casualty Company
Pinebluff Sanitarium
Riker Laboratories, Inc.
R. H. Robins Company
Schering Corporation
G. D. Searle & Co.
Smith, Kline, & French
E. R. Squibb & Sons
Tidewater Hospital
United Fruit Company
Upjohn Company
Wachtel's Physician Supply Co.
Walker Laboratories
Wallace Laboratories
Waverley Sanitarium, Inc.
Westbrook Sanatorium
Winchester Surgical Supply Co.
Winthrop Laboratories, Inc.
World Insurance Company